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## VASCULAR ARCHITECTURE OF THE LESIONS OF MULTIPLE SCLEROSIS

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A relationship between the location of the lesions of multiple sclerosis and the veins of the nervous system was pointed out by Rindfleisch.<sup>1</sup> The majority of those who have dealt with the subject have agreed that small lesions usually surround small veins and that larger plaques probably arise by coalescence. A similar relationship between lesions and veins in cases of "post-infectious encephalomyelitis" has recently been pointed out by Finley.<sup>2</sup> In other papers of this series the probable cause for such a relationship has been traced. Veins in the neighborhood of sclerotic plaques are often found to be engorged, tortuous, surrounded by blood pigment, thrombosed or obstructed. Thrombosis of veins in the central nervous system invariably produces lesions of the same general type as those seen in "encephalomyelitis" and multiple sclerosis. Presumably, therefore, the vascular abnormality is primary to the parenchymal lesions.<sup>3</sup> It is the purpose of the present investigation to make an accurate study of the changes in vascular architecture and the spatial relationships of blood vessels to sclerotic plaques.

### METHODS OF STUDY

Three typical plaques, chosen for their convenient size and position and on the basis of certain obvious technical considerations from material from fourteen persons with multiple sclerosis, were reconstructed as glass plate models.

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This is the eleventh of a series of papers for which the expenses were defrayed by the Multiple Sclerosis Fund of Harvard University.

1. Rindfleisch: Histologische Detail zu der grauen Degeneration von Gehirn und Rückenmark, Arch. f. path. Anat. **26**:474, 1863.

2. Finley, K. H.: Perivenous Changes Present in Acute Encephalitis Associated with Vaccination, Variola and Measles, Arch. Neurol. & Psychiat. **37**: 505 (March) 1937.

3. Putnam, T. J.: Evidences of Vascular Occlusions in Multiple Sclerosis and "Encephalomyelitis," Arch. Neurol. & Psychiat., to be published.

The technic of transparent reconstruction has recently been reviewed by Thomée.<sup>4</sup> Serial paraffin sections, 10 microns thick, were cut through the plaque to be studied. They were stained by various methods, of which Mallory's connective tissue stain appeared the most satisfactory, in that it gave a ready differentiation of myelin, gliosis, vessel walls, red cells, platelets and fibrin. Sections were taken from the series at regular intervals, which depended on the enlargement proposed. They were enlarged by photography to the proper size, and the outlines of the plaques and of the blood vessels were traced in colors on a glass plate 5 by 7 inches (12.7 by 17.7 cm.). Details, such as the presence of thrombi, were verified under the microscope. The glass plates were spaced at the calculated distance by thin strips of glass and taped together. The completed model was photographed. A line drawing was made in ink on a print with reference to the original slides, and the photographic image was bleached out.

Reconstructions of sclerotic plaques have been reported by Dawson,<sup>5</sup> Anton and Wohlwill<sup>6</sup> and Falkiewicz.<sup>7</sup> All three came to the conclusion that the plaque surrounds a large vein like a sleeve and often follows its branchings. No detailed descriptions and no illustrations have been published.

The impression gained from the reconstructions—from which subjective interpretations cannot be excluded—was confirmed by a study of two brains from persons with multiple sclerosis in which the blood vessels were injected after removal from the skull. The injection was unusually poor in spite of the fact that it was promptly carried out, in one instance under ideal conditions, apparently because of prompt clotting of the blood. A few plaques were fairly well filled, however. The vascular pattern was further demonstrated in these and other cases by the benzidine<sup>8</sup> stain and Mallory's stain.

The normal vascular pattern in various parts of the brain is, of course, familiar from the work of Pfeifer,<sup>10</sup> who recently described an apparently characteristic capillary lesion in cerebral tuberculosis.<sup>11</sup> Otherwise, practically no studies of pathologic capillary architecture have been published. Alexander and Putnam<sup>12</sup> have described a reconstruction of a thrombosed vein with the demyelination and perivascular hemorrhage which the obstruction has produced, and Campbell, Alex-

4. Thomée, S.: Ueber Glasrekonstruktion, Ztschr. f. wissenschaftl. Mikr. **45**: 356, 1928.

5. Dawson, J. W.: The Histology of Disseminated Sclerosis, Tr. Roy. Soc. Edinburgh **50**:517, 1916; Edinburgh M. J. **16**:229, 1916.

6. Anton, G., and Wohlwill, F.: Multiple nicht eitrige Encephalomyelitis und multiple Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **12**:31, 1912.

7. Falkiewicz, T.: Zur Pathogenese der multiplen Sklerose, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **28**:172, 1926.

8. Footnote deleted by the author.

9. Lepehne, G.: Zerfall der roten Blutkörperchen beim Ikterus infektiosus, Beitr. z. path. Anat. u. z. allg. Path. **65**:183, 1919. Pickworth, F. A.: A New Method of Study of the Brain Capillaries and Its Application to the Regional Localization of Mental Disorder, J. Anat. **69**:62, 1934.

10. Pfeifer, R. A.: Grundlegende Untersuchungen für die Angioarchitektonik des menschlichen Gehirns, Berlin, Julius Springer, 1930.

11. Pfeifer, R. A.: Kreislauf und Hirntuberkulose, Leipzig, Theodor Steinkopff, 1935.

12. Alexander, L., and Putnam, T. J.: Thrombosis of Small Cerebral Vessels and Its Results, to be published.

ander and Putnam<sup>13</sup> have in preparation at the time of writing a series of observations on a variety of neuropathologic lesions studied by means of the benzidine stain.

#### DESCRIPTION OF THE RECONSTRUCTED MODELS

The first model enlarged 35 diameters in each dimension (figs. 1 and 2) was taken from a patient whose history was unknown but whose condition was pathologically typical of multiple sclerosis of long standing. Numerous plaques, characterized by complete loss of myelin, with sometimes greater, sometimes less gliosis, were scattered through the hemispheres and the brain stem. Practically the entire wall of the lateral ventricles was lined with gliotic tissue in which lay large veins, many of them surrounded by hematogenous pigment. The sclerotic tissue followed the radial veins for a variable distance, and irregular patches of sclerosis were found at intervals along them. The block chosen for reconstruction was taken from the border of one occipital horn, which can be seen at the top of figures 1 and 2. The periventricular gliosis, which was dense, is shown by slight shading in the photograph and by punctate stippling in the drawing. It extended along the border of the ventricle beyond the limits of the block, and perpendicular to it a large dilated vein leading toward the cortex was surrounded by a sleeve of plaque. About two thirds of the distance to the bottom of the section, a branch was given off at right angles (fig. 3). At the juncture of the two a thrombus consisting of agglutinated platelets and a mass of fibrin containing leukocytes was found (fig. 4). It was the only thrombus found in this particular brain, of which a limited amount of tissue was available. Just distal to the thrombus a more or less spherical patch of fresh degeneration occurred (shown in figure 2 by annular stippling). Other older plaques surrounded the larger trunks at intervals. One of these contained a rich, almost angiomatic plexus of capillaries. Particularly striking was the irregular, tortuous, congested contour of the main veins. The whole picture bore a striking resemblance to the reconstruction of Alexander and Putnam.<sup>12</sup>

The second reconstruction (figs. 5 and 6), enlarged 20 diameters in each dimension, was made from the brain of a patient with multiple sclerosis which had run a typical course for twelve years, who had died in an exacerbation. In this case there were a striking number of fresh plaques as well as many old ones in the hemispheres. Periventricular gliosis was unusually slight. Typical plaques were found scattered through the brain stem. The block chosen was taken from the white matter of one parietal lobe and included portions of an old and a fresh plaque and several thrombosed veins. The most intense gliosis, containing a large plexus of capillaries, is shown in heavy punctate stippling about one third of the way from the bottom of the drawing. It was

13. Campbell, A. C. P.; Alexander, L., and Putnam, T. J.: The Vascular Pattern in Various Lesions of the Human Central Nervous System, to be published.



Fig. 1.—Photograph of the first model. The pile of glass plates is viewed at a slightly oblique angle. The walls of the blood vessels are shown as black lines. The extent of the plaques, shown in green in the original model, appears as a slight gray cloud in the photograph. Original enlargement, 35 diameters.

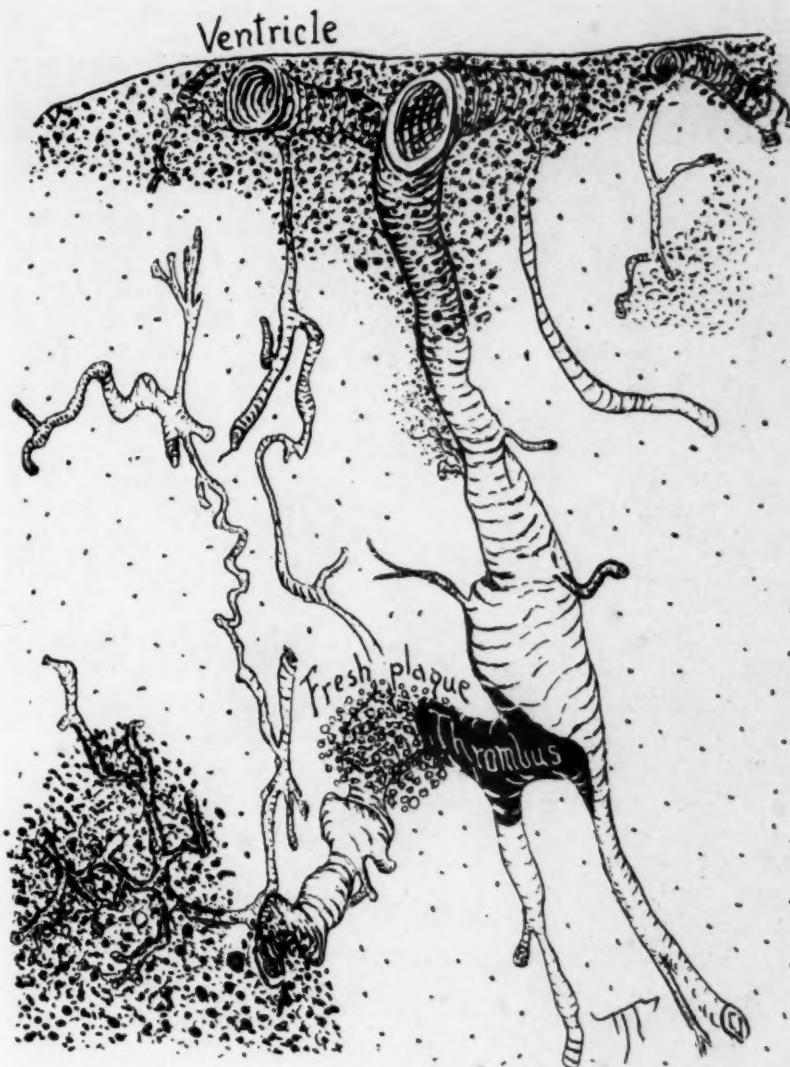


Fig. 2.—Interpretation of the photograph shown in figure 1, in line drawing. Blood vessels are represented as hollow tubes, except where the thrombus occurs, which is represented in black with white shading. Dense old plaques are shown in punctate stippling, with the convention that larger dots represent more superficial plates of glass. Fresh areas of degeneration (without fibrous gliosis) are shown by annular stippling, heavier rings marking the more superficial layers. Notice that the freshest plaque appears about a vein between a fresh thrombus and a dense, congested old plaque.



Fig. 3.—Photomicrograph of one of the sections from which the model was constructed. The area shown in the reconstruction is enclosed by lines. Mallory's connective tissue stain; original enlargement  $\times 5$ .

surrounded by a zone of fresher degeneration (shown by annular stippling) in which smaller thrombosed veins occurred. A zone of more or less normal, relatively avascular, tissue separated this old plaque from a fresher one above, in which lay a large thrombosed vein. The photograph gives a more plastic idea than the drawing of the great vascularity of the old plaque. The old gliotic plaque, the fresh degeneration and some of the thrombi are shown in figure 7.

The third reconstruction (fig. 8), enlarged 40 diameters, from a patient showing a typical histologic picture of multiple sclerosis, adds nothing further to what is shown in the other two. The characteristic dilatation and tortuosity of the main vein and the dense capillary net-



Fig. 4.—Photomicrograph of the platelet and fibrin thrombus represented in the reconstruction. Oil immersion.

work are clearly shown. No thrombi and no areas of fresh degeneration were observed in this block.

DESCRIPTION OF THE SECTIONS PREPARED BY THE INJECTION OF  
INDIA INK AND STAINING BY THE BENZIDINE METHOD

Figures 9 and 10 show the vessels in plaques at the angle of the ventricle in two different cases of multiple sclerosis injected with india ink. In the specimen illustrated in figure 9 the injection was incomplete and a benzidine stain was superimposed on it. Figure 11 shows a periventricular area from a normal brain prepared in the same way for comparison with figure 10. The work of Pfeifer<sup>10</sup> shows many more

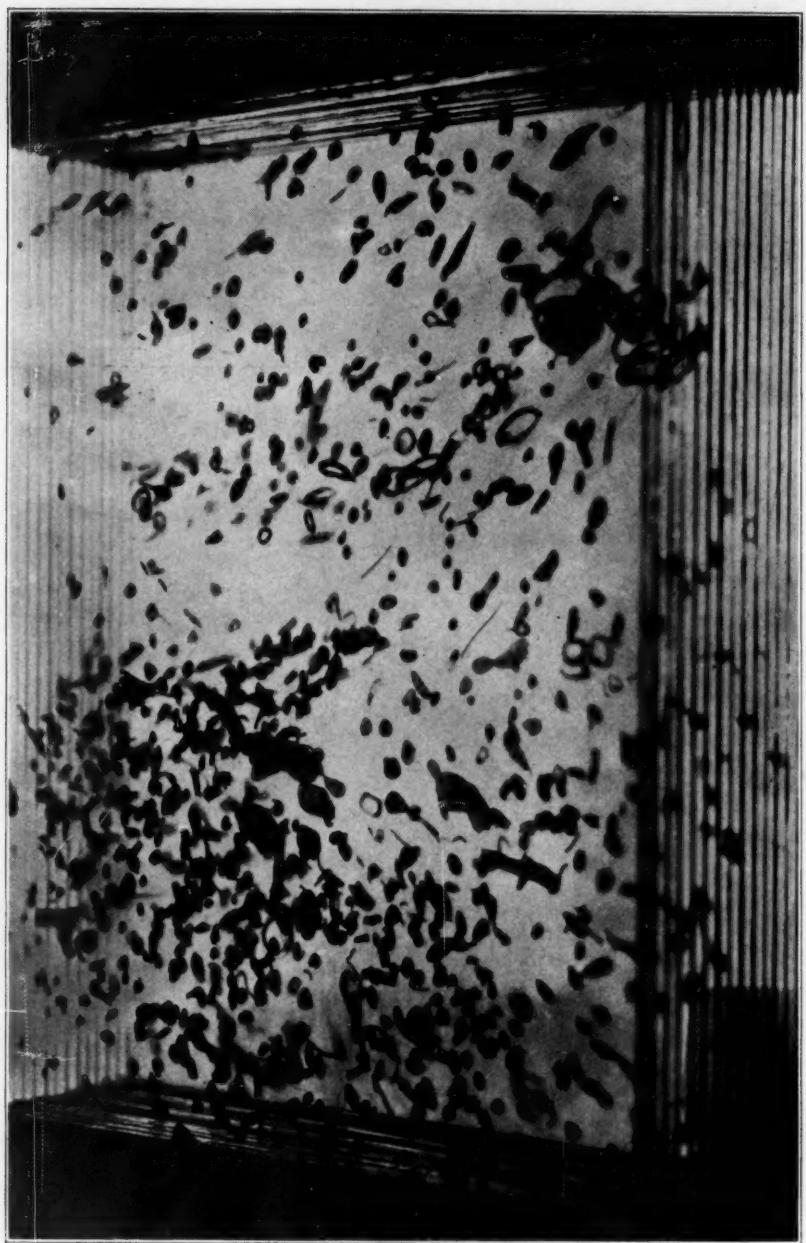


Fig. 5.—Photograph of the second model. The outlines of the plaques show faintly, but their location is clearly marked by the enormous congestion. Thrombosed vessels are rather indistinctly shown as solid dark areas. Original enlargement  $\times 20$ .

normal specimens. Such preparations do not show the relationship of the vessels to the plaques, but they constitute further examples of the characteristic gnarled vessel trees and engorgement illustrated by

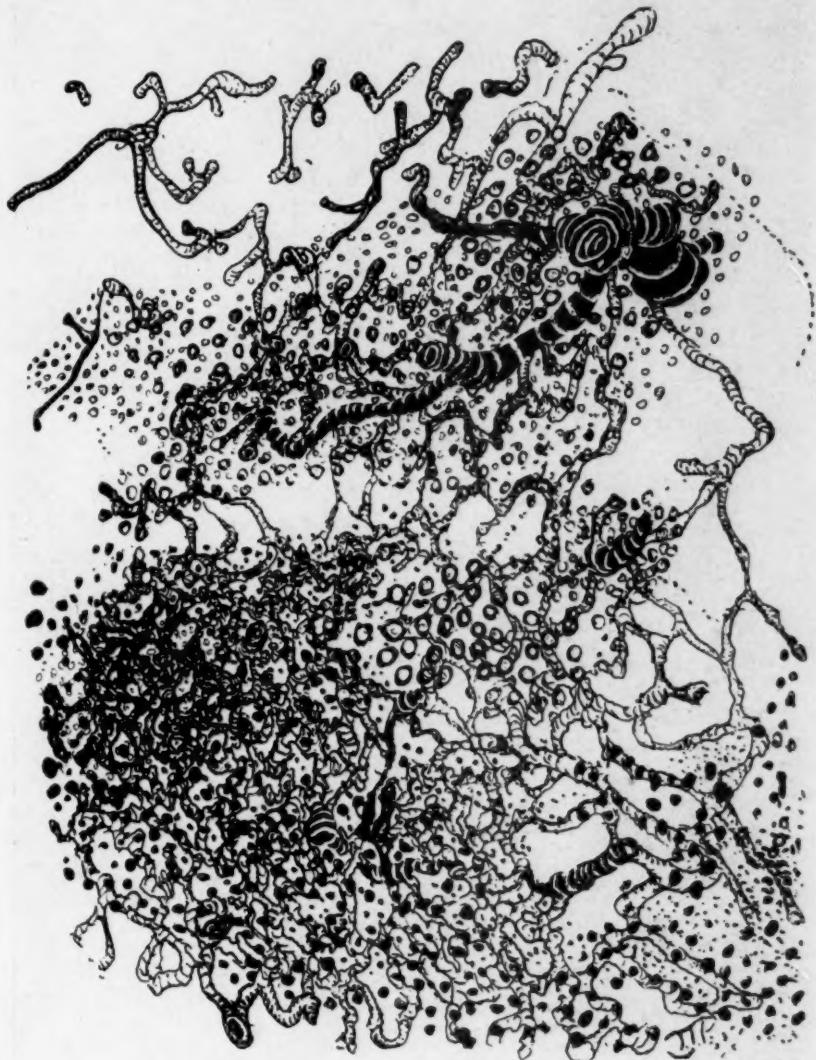


Fig. 6.—Linear interpretation of the photograph shown in figure 5. The notation is similar to that of figure 2.

the reconstructions. The abnormality is typical and obvious. The nearest analogy to it is seen in some of the vascular lesions studied by Campbell, Alexander and Putnam.<sup>18</sup>



Fig. 7.—Photomicrograph of one of the sections used for the second enlargement. Mallory's connective tissue stain; original enlargement  $\times 20$ .



Fig. 8.—Photograph of the third model. In this block, no thrombi and no fresh lesions were found. Original enlargement  $\times 40$ .

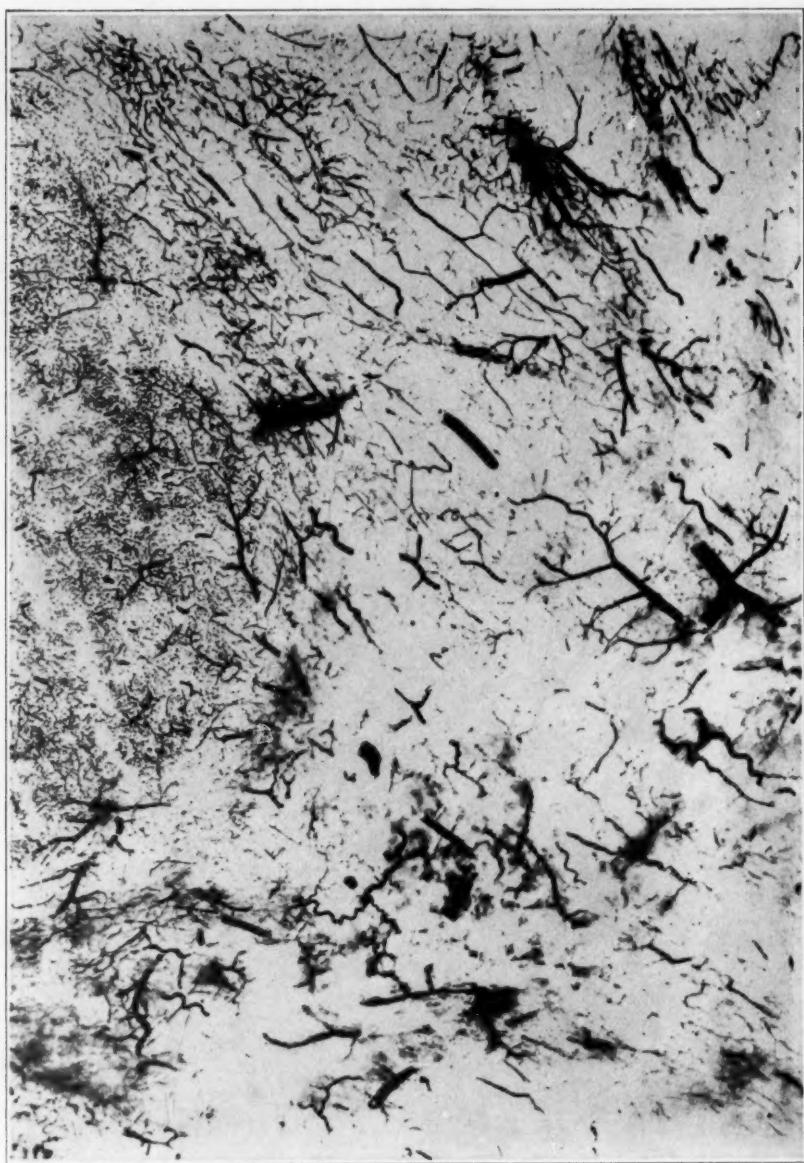


Fig. 9.—The blood vessels in the white matter of the occipital lobe of a patient with multiple sclerosis. The blood vessels of the brain were injected after removal from the skull. As the injection was incomplete, it was supplemented by the benzidine stain. Section 100 microns thick; original enlargement  $\times 10$ .

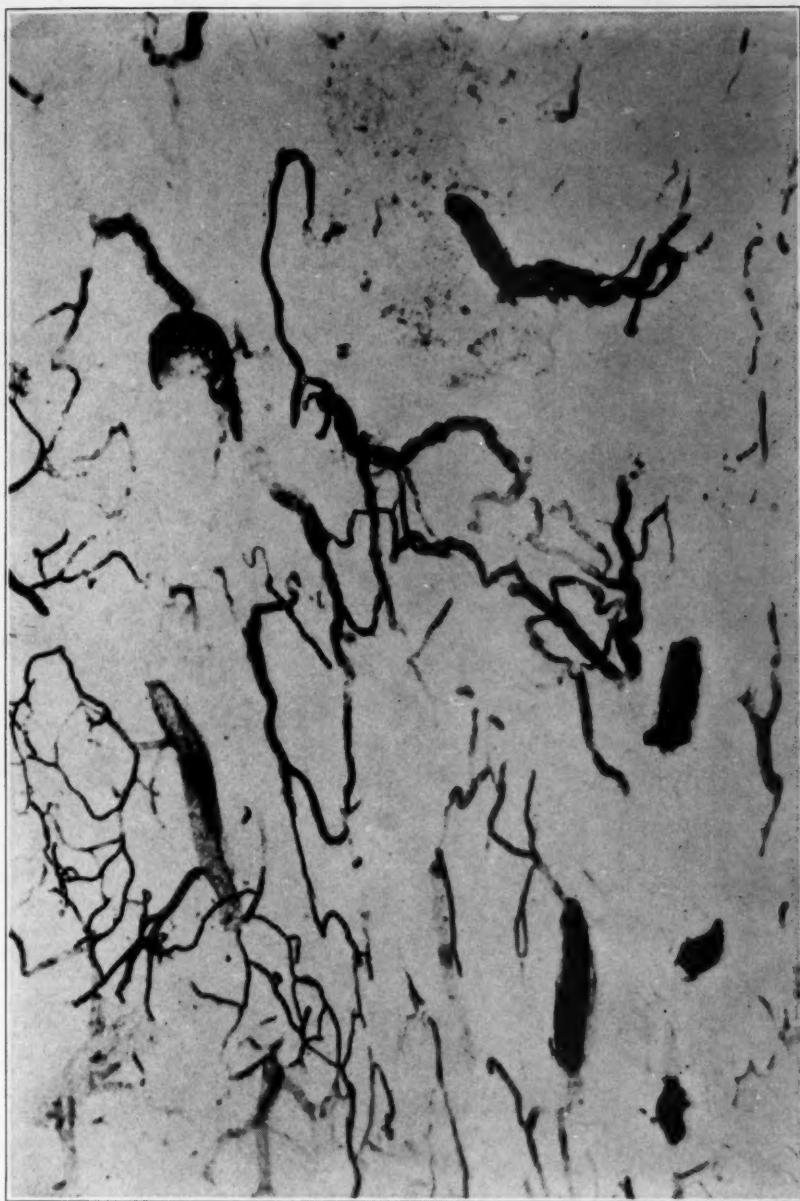


Fig. 10.—The blood vessels in a sclerotic plaque in a characteristic location at the angle of the lateral ventricle. From the brain of a patient with multiple sclerosis, injected with india ink after removal from the skull. Section 100 microns thick, unstained; original enlargement  $\times 35$ .



Fig. 11.—Angle of the lateral ventricle from the brain of a "normal" adult, injected after removal from the skull, for comparison with the preparation shown in figure 10. Section 100 microns thick; original enlargement  $\times 35$ .

## SUMMARY

Three glass plate reconstructions and two specimens showing the vascular pattern of plaques of multiple sclerosis are presented.

The vascular architecture of the lesions of multiple sclerosis is characteristic. Small plaques tend to surround engorged veins, which are gnarled and tortuous. If a thrombus occurs in a vein, an area of fresh degeneration appears in close relation to it. There is usually an increase of capillaries in sclerotic plaques, but a decrease may also occur.

## RELATIONSHIP OF THE AUTONOMIC NERVOUS SYSTEM TO PATHOGENESIS OF EPILEPSY

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Long ago, Nothnagel<sup>1</sup> and Hughlings Jackson<sup>2</sup> suggested vasoconstriction as the cause of epileptic seizures. However, it was only after the epoch-making histopathologic studies of Spielmeyer<sup>3</sup> and his school, demonstrating functional vasospasm as the underlying pathoanatomic change in the epilepsies, that their point of view received strong support. Long before that time many observers at the operating table had reported shrinking and anemia of the brain at the onset of and during an epileptic seizure, and following it edema with injection of the cortical vessels (Sargent, Cushing, Leriche, Foerster and Marburg, cited by Krause and Schum<sup>4</sup>). During encephalography there were also observed at the onset of an epileptic seizure a sudden fall in the pressure of the cerebrospinal fluid and then a definite rise—phenomena pointing toward vasoconstriction and vasodilation. Finally, there appeared the conclusive observations of Penfield<sup>5</sup> on the behavior of the meningeal and the cortical blood vessels during an attack produced in man by electrical stimulation. The importance of these observations in the elucidation of the pathogenesis of epileptic attacks is equal to that of the histopathologic studies of Spielmeyer.

The part played by vasomotor disorders in the pathogenesis of epileptic seizures justifies me in dealing in this paper at some length with autonomic disturbances and, especially, with the vasomotor changes observed in epilepsy.

An epileptic seizure is the most important manifestation of a vascular crisis which not only occurs in the pial and the cerebral blood vessels but a more generalized disturbance, affecting chiefly the blood

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Read at the Second International Neurological Congress, London, July 29, 1935.

1. Nothnagel, H.: *Virchows Arch. f. path. Anat.* **44**:1, 1868.
2. Jackson, Hughlings: *West Riding Asylum Rep.* **3**:334, 1873.
3. Spielmeyer, W.: *München. med. Wochenschr.* **47**:1424, 1922; *Ztschr. f. d. ges. Neurol. u. Psychiat.* **148**:285, 1933.
4. Krause, F., and Schum, H.: *Die epileptischen Erkrankungen, ihre anatomischen und physiologischen Unterlagen sowie ihre chirurgische Behandlung*, in Krause, F.: *Die spezielle Chirurgie der Gehirnkrankheiten*, Stuttgart, Ferdinand Enke, 1931, vol. 2.
5. Penfield, W.: *Ann. Int. Med.* **7**:303, 1933.

vessels of the heart. This conception is in accord with the close relationship recognized by pharmacologists between cardiac and cerebral blood vessels and with observations at autopsy of epicardial and endocardial hemorrhages in cases of cerebral vascular lesions. Neubürger's<sup>6</sup> observations on idiopathic, as well as symptomatic, epilepsy showed that in epileptic seizures the whole circulatory system may be affected. According to him the lesions noted in the cardiac muscle in young patients with epilepsy are of a functional nature, attacking principally the small blood vessels. One might assume that there is associated with an epileptic seizure an attack of closure of the cardiac vessels, producing in the cardiac muscle the same destructive lesions as does a genuine attack of angina pectoris. Frisch,<sup>7</sup> Hiller<sup>8</sup> and Stemmer and Gruber and Lantz<sup>9</sup> (cited by Stauder<sup>10</sup>) reported similar observations, both from an anatomic and from a clinical point of view, of more or less typical complaints of angina pectoris in twenty of sixty cases of epilepsy. Padilla and Cossio<sup>11</sup> demonstrated cardiographically cessation of the heart beat at the beginning of an epileptic seizure; Winternitz<sup>12</sup> showed the same phenomenon after status epilepticus; Eufinger and Molz<sup>13</sup> noted during an attack changes in the electrocardiogram comparable to those observed in cases of coronary occlusion. Josephson and Teplitz<sup>14</sup> saw spasm of the cardiac muscle during the tonic phase of an epileptic seizure and dilatation of the right side of the heart afterward. They said that the râles and the foam seen in the mouths of patients with epilepsy were symptoms of transitory edema of the lungs. Here belong also the observations of Etienne<sup>15</sup> and Penfield<sup>5</sup> on the disappearance of the radial pulse during a seizure.<sup>16</sup>

Pinczewski<sup>17</sup> reported the case of a man aged 25 who suffered from jacksonian attacks on the right side and had complained for one year

6. Neubürger, K.: Frankfurt. Ztschr. f. Path. **46**:14, 1933.
7. Frisch, F.: Das vegetative System der Epileptiker, Berlin, Julius Springer, 1928.
8. Hiller, F.: München. med. Wchnschr. **79**:1465, 1932; **80**:1515, 1933.
9. Gruber and Lantz, quoted by Stauder.<sup>10</sup>
10. Stauder, K. H.: Arch. f. Psychiat. **102**:456, 1934.
11. Padilla, T., and Cossio, P., Jr.: Zentralbl. f. d. ges. Neurol. u. Psychiat. **58**:693, 1930.
12. Winternitz, M.: Med. Klin. **29**:1080, 1933.
13. Eufinger, H., and Molz, H.: Klin. Wchnschr. **13**:1177, 1934.
14. Josephson and Teplitz, quoted by Stauder.<sup>10</sup>
15. Etienne, G.: Rev. neurol. **1**:1317, 1932.
16. I remember an impressive case of a young woman physician, with a healthy heart, who suffered from rare but severe epileptic attacks who, after a long interval free from attacks, died suddenly of heart block. I consider this case one of cardiac localization of an epileptic angioneuropathic tendency.
17. Pinczewski, Neurol. polska **15**:294, 1933; abstr., Zentralbl. f. d. ges. Neurol. u. Psychiat. **68**:649, 1933.

of intermittent claudication of the right leg. Not long ago, I observed a man who had been suffering for twelve years from organic epilepsy. A soldier in the World War, he had lain for several hours in the snow before his first attack, which seized him the moment he entered a warm room. The attacks, which now come several times a year, are ushered in by prodromal symptoms lasting sometimes a few days, during which he feels apathetic and slow. He has difficulty in thinking; the fingers of the right hand always become "dead," and there is often a scintillating scotoma. The anemia of the fingers often lasts several hours, and then disappears and recurs until the onset of the attack, which starts always in the left leg and rapidly becomes generalized, with loss of consciousness. After the attacks the patient feels very weak and often remains in bed for from two to four weeks.

Stauder<sup>10</sup> was probably right when he attributed to vasomotor disturbances the various disorders of the vestibular apparatus and the perimetric and campimetric changes which occur in epileptic attacks.

In view of these facts, it is not unlikely that some curious vasomotor states observed in patients affected with seizures are in reality an expression of their angioneurotic constitution and not necessarily epileptic attacks.

It is probable that in some cases the condition wrongly called "late epilepsy" is the result of hypertension, especially the fleeting form of this disease, so often associated with functional vasoconstriction (Krapf's<sup>18</sup> hypertonic epilepsy). It is noteworthy that Marx and Weber<sup>19</sup> claimed sometimes to have observed high blood pressures, even in young epileptic patients in the resting state. From my personal experience, however, I am unable to confirm their assertion. In this connection, as well as in regard to the production of seizures by means of retention produced by pitressin, one can find in the literature a great deal of discussion on the possibility that hormones of the posterior pituitary gland, or analogous pressor substances, may circulate in the blood serum and produce spontaneous epileptic seizures.

Finally, I must mention briefly some studies of the sinus caroticus, which is thought to provide an actual mechanism for vagus pressure reflexes, thus constituting a regulatory center for the reflexes of the cerebral blood vessels. To the present, however, neither the sinus caroticus nor the near-by carotid gland has been demonstrated to be important. The therapeutic extirpation of both, performed in patients with epilepsy, was unsuccessful in the majority of cases (Marinesco

18. Krapf, E.: Arch. f. Psychiat. **93**:409, 1931.

19. Marx, H., and Weber, P.: Nervenarzt **7**:183, 1934.

and Kreindler;<sup>20</sup> Marinesco, Kreindler and Bruch;<sup>21</sup> Lauwers;<sup>22</sup> Rizzatti;<sup>23</sup> Danielopolu and Marcu;<sup>24</sup> Guibal and Ramé;<sup>25</sup> Josephson and Teplitz,<sup>14</sup> and others).

If on the basis of the observations of Spielmeyer<sup>3</sup> and Penfield<sup>5</sup> one accepts vasospasm as the precipitating factor in epileptic seizures, one must then seek the nociceptive agents which, on the one hand, increase the convulsive liability of the vasomotor nerves and nerve cells and, on the other, liberate the final stimulus which produces the ischemia and excitation of the brain.

One is at once inclined to see these agents in the pathologic states of the autonomic nervous system and the endocrine glands. Disorders of the former might become evident in changes of its tonus, demonstrable by its behavior toward various pharmacologic substances. On the other hand, one has here all kinds of metabolic disorders (disturbances in water, mineral, gas, carbohydrate, fat and nitrogen metabolism; disorders of the acid-base equilibrium; abnormal behavior of the enzymes of the blood; hematologic and serologic changes; toxicity of the urine, etc.), as well as the different hormonal abnormalities. If some of these pathologic states should appear a short time before the onset of an attack and in a considerable number of cases, one could then attribute to them a certain value in the pathogenesis of epileptic attacks or of epileptic disease. However, although a great deal of intelligent and sincere research has been done to solve this problem, up to the present it seems to me that the results of this work are contradictory, inconstant, unimportant or negative. Consequently, I need not consider them in this paper at length. In the present state of knowledge the positive results of these studies point only toward an accessory rôle of the disorders mentioned in the pathogenesis of epilepsy. One must, further, keep in mind that most of them are observed in other diseases, as, for instance, in typical migraine, and, finally, that analogous changes are probably evident in all kinds of pathologic states of the autonomic nervous system and often also in normal persons. One must, therefore, consider even the retention of water which occurs before a seizure frequently, but by no means invariably, as only an accessory agent in the production of epileptic attacks.

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20. Marinesco, G., and Kreindler, A.: *Klin. Wchnschr.* **9**:2204, 1930.
21. Marinesco, G.; Kreindler, A., and Bruch, A.: *Ztschr. f. d. ges. exper. Med.* **79**:333, 1931.
22. Lauwers: *Zentralbl. f. d. ges. Neurol. u. Psychiat.* **61**:605, 1931.
23. Rizzatti: *Zentralbl. f. d. ges. Neurol. u. Psychiat.* **64**:789, 1932.
24. Danielopolu, D., and Marcu, I.: *Wien. klin. Wchnschr.* **45**:457, 1932.
25. Guibal, J., and Ramé, A.: *Bull. et mém. Soc. nat. de chir.* **59**:717, 1933.

So far, I have not dealt fully with the only constant phenomena encountered in epilepsy, namely, the vasomotor manifestations taking place in the pial and the cerebral blood vessels. According to Penfield,<sup>5</sup> they are of constant appearance in organic epilepsy during, and often after, an attack which has been induced by galvanic or faradic stimulation of the human cortex. Penfield<sup>5</sup> reported forty-three cases, in fourteen of which electrical stimulation did not produce an attack and in which he did not observe any vasomotor changes. In four of the last-mentioned cases there appeared only an aura and no vasomotor phenomena. In the other twenty-six cases there were definite vasomotor changes, which in twenty instances persisted after the attack. In most of these twenty-six cases arterial pulsation ceased during the seizure frequently over a wide area of the brain. The arteries sometimes took on the appearance of veins and became dark blue. After the seizure the arteries began to pulsate again with unusual strength, and sometimes the veins then took on an arterial hue. In these last cases, either the blood passed quickly through the widely open capillary bed or the brain tissue had become unable during that time to absorb the oxygen from the blood. More often, however, Penfield observed in fit-producing areas localized anemia instead of vasodilatation after the attack. He<sup>5</sup> stated that it is probable that these anemic areas which appear after convulsions are the basis of some postepileptic pareses. Twice he noticed the spontaneous appearance of such anemic areas, and once, arterial vasoconstriction without any stimulation, but without the production of an attack; six times there was after an attack complete spasmodic occlusion of one or more pial arteries, lasting from fifteen to thirty minutes. It is evident from this that local vasomotor reflexes can take place in the brain of the epileptic subject—a phenomenon which has never been described in the normal brain and which could not be reproduced in laboratory animals.

It is striking that acetylcholine, which is an energetic vasodilator of the pial arteries (Wolff<sup>26</sup>), has no effect on the course of idiopathic epilepsy (Bertaglia,<sup>27</sup> Lloyd,<sup>28</sup> McLaughlin,<sup>29</sup> de Gennes<sup>30</sup> and I<sup>31</sup>), in which one might expect, perhaps, analogous angiospastic phenomena. However, the absence of such an effect should not be surprising, as theoretically the use of acetylcholine is indicated only at the onset of an

26. Wolff, H. G.: The Cerebral Circulation: XI a. The Action of Acetylcholine, *Arch. Neurol. & Psychiat.* **22**:686 (Oct.) 1929.

27. Bertaglia, G.: *Zentralbl. f. d. ges. Neurol. u. Psychiat.* **69**:214, 1934.

28. Lloyd, J. E. S.: *Zentralbl. f. d. ges. Neurol. u. Psychiat.* **69**:489, 1934.

29. McLaughlin, F. L.: *Zentralbl. f. d. ges. Neurol. u. Psychiat.* **69**:489, 1934.

30. de Gennes, L.: *Bull. et mém. Soc. méd. d. hôp. de Paris* **48**:394, 1932.

31. Orzechowski, K.: *Rocznik psychiat.*, 1929, no. 16, p. 1.

expected vasospasm, i. e., during an aura of longer duration than usual. There is therefore, according to my personal experience and that of others (de Gennes,<sup>30</sup> Pagniez, Plichet and Decourt<sup>32</sup> and Bolsi<sup>33</sup>), no doubt that in many cases of severe status epilepticus injection of acetylcholine or encephalography might be a life-saving procedure, by terminating the status which is the expression of a permanent vasospasm of the cerebral blood vessels. (The frequent occurrence of a low pressure of the cerebrospinal fluid suggests the possibility of introducing into the subarachnoid space larger quantities of air during encephalography.)

According to Penfield,<sup>5</sup> epileptogenic vasoconstriction depends neither on the cervicodorsal portion of the sympathetic trunk nor on the cerebral part of the parasympathetic system (Gage<sup>34</sup>), but seems to be a sequel of abnormal reflexes taking place in the nerve cells on the wall of the pial blood vessels or in the local vascular nerve plexuses.

Penfield's observations, which do not explain the mechanism of the spontaneous seizures of idiopathic epilepsy, can nevertheless be looked on as the most interesting experimental contribution to the problem of human epilepsy. It is known from some studies that an epileptic seizure can be induced even by the slightest chemical disorder. It is not surprising, therefore, that a relatively strong electric stimulus, when applied to a diseased brain, produces a seizure, especially when one bears in mind that such stimulation produces striking vasomotor changes in the brain. It is known, on the other hand, from the studies of Spielmeyer's school that almost all pathologico-anatomic changes in all forms of epilepsy are to be explained by preceding vasospasms. These vasospasms, according to Penfield, are frequent sequelae of epileptic seizures induced experimentally in the human brain and are analogous to the seizures affecting the patient spontaneously. Cure of the disease is obtained in certain cases by extirpation of the affected vessels, together with the involved portion of the brain (Penfield<sup>35</sup>). It is improbable that the vasospasms occurring in an epileptic seizure are only secondary phenomena. On the contrary, Penfield's experimental findings form the final link in the chain of evidence which points toward functional vasomotor disorder as the primary etiologic factor in all epileptic seizures, including those of idiopathic epilepsy. In cases of the last type the same pathologic changes of a vascular character are shown. Conse-

32. Pagniez, P.; Plichet, A., and Decourt, P.: Bull. et mém. Soc. méd. d. hôp. de Paris **48**:424, 1932.

33. Bolsi, D.: Rev. neurol. **1**:1321, 1932.

34. Gage, L., quoted by Penfield.<sup>5</sup>

35. Penfield, W.: Epilepsy and Surgical Therapy, Arch. Neurol. & Psychiat. **36**:449 (Sept.) 1936.

quently, one should now localize the anatomic substratum of the tendency to epilepsy, the *aptitude convulsive*, in the nerve plexuses of the pial and the cerebral blood vessels.

Most often, the irritative process is situated in the leptomeninges carrying the large and medium arteries to the cerebral cortex. In cases of symptomatic epilepsy this irritative agent may be observed in a pathologic change of the leptomeninges or the brain substance, affecting also the meninges. In cerebral lesions which do not include the pia mater, the pathologic process spreads through the perivascular spaces, thus stimulating the vasomotor nerves and inducing an epileptic seizure. This is why in so many extensive cortical processes, such as Alzheimer's and Pick's disease—in which, at least in the beginning, the leptomeninges and the perivascular spaces are free from morbid change—epileptic seizures are rarely observed. In the rather frequent cases of meningeal cicatrix or of other meningeal lesions without epileptic manifestations, if the underlying cortex is sufficiently normal to respond with seizures, the pathologic change either does not stimulate the vasomotor nerves or destroys them, leaving the blood vessels denervated.

The question arises now as to what may be the nature of the stimulus originating in the cicatrix of the leptomeninges and in the meningeal reduplications (perivascular spaces and pacchionian granulations). The effect of pressure of the lesion, which one is often inclined to accept as the provocative agent, is rarely present, and its rôle in connection with epilepsy is, at any rate, not definitely demonstrated. It seems more likely that the vasomotor nerves are stimulated by the contracting cicatrix.

It seems to be most probable that the meningocortical epileptogenic factor is chiefly of a chemical nature. It is likely that the nociceptive agent will be found in the cerebrospinal fluid of the meningeal cicatrix and the perivascular spaces or in the fluid replacing the cerebrospinal fluid. Whatever the structure of a meningeal lesion may be, it usually compresses the circulatory spaces of the cerebrospinal fluid, producing local stagnation and chemical changes in its composition, more or less comparable to those observed, or assumed to be present, in the cerebrospinal fluid in cases of spinal block due to extramedullary tumor. I think, therefore, that the source of the irritative agent must be looked for in the pathologic substances of the cerebrospinal fluid, attacking the vasomotor nerves through the perivascular spaces and producing in them a permanent state of irritation. However, if the leptomeningeal cicatrix is of such nature as to allow free circulation of the cerebrospinal fluid, then, in spite of meningocortical adhesion, epilepsy is absent. If the vasomotor nerves are destroyed in a leptomeningeal cicatrix, even a local collection of fluid cannot produce epilepsy.

This point of view could, in my opinion, throw light on what is assumed to be the anatomic substratum of idiopathic epilepsy. If this hypothesis is correct, one must search for the irritating agent in idiopathic epilepsy also in the nerve plexuses of the blood vessels, i. e., chiefly in the leptomeninges. The meningeal lesion responsible for idiopathic epilepsy could have such structure as to be invisible with present methods of investigation or could be so commonly observed as to be judged unimportant. Finally, the production of the substance could be reversible and therefore absent at the time of operation or at autopsy.

The hypothesis of the anatomic nociceptive agent of idiopathic epilepsy, presented by me at the annual meeting of Polish psychiatrists in 1929, was elaborated from the following evidence: (1) complete clinical analogy between idiopathic epilepsy and other forms of the disease, especially posttraumatic epilepsy, in which a meningeal lesion is usually the most important irritative agent; (2) collections of cerebrospinal fluid in the leptomeninges, which are too frequently observed in the course of idiopathic epilepsy to be considered unimportant, and (3) improvement after encephalography.

I am still inclined to accept the local or generalized circulatory changes of the cerebrospinal fluid as the origin of seizures in idiopathic epilepsy. I consider that in this disease the leptomeninx is either totally or partially abnormally developed, in consequence of which, owing either to a greater number of arachnoid trabeculae than usual or to their abnormal thickness and shortness, there result slowing and stagnation of the circulation of cerebrospinal fluid. It seems that in the majority of cases of idiopathic epilepsy the leptomeningeal changes are situated on the convexity of the brain; nevertheless, they may be localized sometimes at the base (Dide<sup>36</sup>). The meningeal anomaly may include also the adventitia of the blood vessels, with their nerve plexuses. It is probable also that the cortical perivascular spaces are frequently affected, as judged by the thickening of the adventitia of the cerebral blood vessels.

This constitutionally abnormal structure of the leptomeninges may be compared to some pathologic conditions of the skin, the most striking of which is the trophoedema cutis chronicum hereditarium of Meige.<sup>37</sup> This author expressed the opinion that in this disease the subcutaneous connective tissue and the elastic fibers have such a structure and position as to slow the lymphatic circulation. In an analogous manner, one

36. Dide, M.: Rev. neurol. **1**:1354, 1932.

37. Meige, H.: Nouv. iconog. de la Salpêtrière **12**:453, 1899; **14**:465, 1901.

might speak of hypothetic meningopathy associated with idiopathic epilepsy as *trophoedema leptomeningitis universalis aut circumscriptum*.<sup>38</sup>

The sequel of this usually constitutional anomaly would be, first, slowing of the normal circulation of the cerebrospinal fluid, producing stagnation of various grades, sometimes generalized, sometimes restricted to certain areas of the subarachnoid spaces and at times manifesting itself only just before an attack.

To present microscopic evidence of the existence of meningeal trophedema would be difficult, for various reasons. In the presence of slight changes—and such are probably the rule in idiopathic epilepsy—the trophedema could be observed only during profuse filling of the subarachnoid spaces by the cerebrospinal fluid. In patients with epilepsy this is probably only temporary and to be expected just before an attack. Histologic evidence of leptomeningeal trophedema would be more likely to be observed in cases of idiopathic epilepsy if attention were particularly directed toward this hypothetic change. It is also necessary to point out that the long-known trophedema cutis still awaits a definite histologic explanation. The cysts and other collections of fluid, as well as the thickening of the meninges, observed in some cases of idiopathic epilepsy are probably an expression of leptomeningeal trophedema of a higher grade, and the fact that in some of these cases the disease is considered as symptomatic epilepsy cannot alter this conception.

The slowing of the circulation of the cerebrospinal fluid and of its resorption may be generalized, and not localized to a circumscribed area of the leptomeninges. Further, it may be independent of the leptomeninges, as in cases of congenital or acquired hypoplasia or dysplasia of the choroid plexus and ependyma. This is the point of view of Minkowski,<sup>39</sup> although he generalized too far.

The cerebrospinal fluid enclosed in the area of trophedema by the arachnoid meshes might undergo chemical changes, which would increase the irritability of the vasomotor nerves, until the convulsant threshold was reached. Toxic substances resulting from hormonal abnormalities in persons with epilepsy and carried by the cerebrospinal

38. One cannot exclude a priori the coupling of trophedema of the leptomeninges with an anatomic anomaly of the neuroglia of the superficial cortical layers—which would explain the tendency of the neuroglia to proliferate in cases of epilepsy (Jakob, A.: *Normale und pathologische Anatomie und Histologie des Grosshirns*, Leipzig, Franz Deuticke, 1927. Bielschowsky, M.: J. f. Psychiat. u. Neurol. **21**:1, 1915. Minowski<sup>39</sup>). Some localized cortical lesions considered as the source of epilepsy might have the same origin, i. e., abnormal development of the leptomeninges occurring with dysplasia of the underlying cortex.

39. Minkowski, M.: *Rocznik psychiat.*; 1933, no. 20, p. 225; abstr., *Zentralbl. f. d. ges. Neurol. u. Psychiat.* **68**:651, 1933.

fluid or the blood can associate themselves with such irritating agents. I expressed this view in 1929, in the following words:<sup>31</sup>

Such a collection of toxic substances may precipitate an attack . . . , the substances acting locally on the vasomotor nerves . . . and inducing vasoconstriction preceding the attack.

At that time the existence of the vasomotor nerves, except those on the larger blood vessels, was denied by many investigators. Now, as a result of the studies made by American workers, it is known not only that the smaller pial blood vessels are innervated by sympathetic nerve fibers (Forbes<sup>40</sup>) and parasympathetic fibers (Cobb and Finesinger<sup>41</sup> and Chorobski and Penfield<sup>42</sup>) but that the intracerebral blood vessels have their nerve plexuses (Penfield<sup>43</sup>).

Often, after a typical, and sometimes severe, epileptic attack the patient feels quiet and relieved, as if liberated from oppression. This happens particularly in the first years of the disease and especially after a long interval free from seizures. It is possible that each recurring seizure may produce temporary increase in the circulation of cerebrospinal fluid through the subarachnoid spaces, thus freeing the cortex from accumulated irritating substances. In this way, an epileptic attack may have a mechanical action like that of a suction pump and may be followed by a period during which the brain is less liable to attacks.

There are instances in which there are widespread changes in the pia mater but no epilepsy—for example, cases of obliteration of the subarachnoid spaces following epidemic meningitis and some cases of hydrocephalus. In these instances one finds total fibrosis of the leptomeninges and complete closure of the subarachnoid spaces. The cerebrospinal fluid is absent, as are also the irritative substances which would otherwise stimulate the vascular nerve plexuses. The same is probably true in some instances of dementia paralytica and in cases of meningitis with filling of the perivascular spaces by the cellular exudate.

Epilepsy belongs to a group of seizure diseases characterized by attacks which recur frequently and are often of short duration. In this group I would include epilepsies: pyknolepsy, narcolepsy and catalepsy; the vaguely understood forms of subcortical epilepsy (Sterl-

40. Forbes, H. S.: Cerebral Circulation: I. Observation and Measurement of Pial Vessels, *Arch. Neurol. & Psychiat.* **19**:751 (May) 1928.

41. Cobb, S., and Finesinger, J.: Cerebral Circulation: XIX. The Vagal Pathways of the Vasodilator Impulses, *Arch. Neurol. & Psychiat.* **28**:1243 (Dec.) 1932.

42. Chorobski, J., and Penfield, W.: Cerebral Vasodilator Nerves and Their Pathway from the Medulla Oblongata, with Observations on the Pial and Intracerebral Vascular Plexus, *Arch. Neurol. & Psychiat.* **28**:1257 (Dec.) 1932.

43. Penfield, W.: Intracerebral Vascular Nerves, *Arch. Neurol. & Psychiat.* **27**:30 (Jan.) 1932.

ing<sup>44</sup>) and extrapyramidal epilepsy; dystonic seizures (*familiärer Rindenkrampf* of Rülf<sup>45</sup>) and convulsions due to involvement of the diencephalon (Penfield<sup>46</sup>), and typical migraine. The epilepsies may be defined as an expression of a specific localized angioneurosis or angioneuropathy of the leptomeningeal and the cerebral blood vessels. The anatomic substratum of all forms of epilepsy is therefore, according to this conception: the leptomeninginx, the cerebrospinal fluid, the perivascular spaces and the vasomotor nerves.

Grand mal seizures are not the only manifestation of epilepsy, as the disease may continue for some time with no expression other than loss of consciousness or it may take the form of attacks without the loss of consciousness, as described by Hunt.<sup>47</sup> I have been concerned in this paper principally with a discussion of the mechanism of the most frequently observed and most characteristic symptom of epileptic disease, i. e., the major seizure or grand mal attack, recognizing, however, that the same pathogenesis holds for other types of the epileptic fit.

So-called idiopathic epilepsy is organic in nature. Some authors (Abadie<sup>48</sup> and Klessens<sup>49</sup>) accepted the hypothesis that the cause in some cases of the idiopathic form is to be looked for in extracranial organs (circulatory and pleural epilepsy). It is unnecessary even in such types to accept a special ictophilic constitution of the brain.

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44. Sterling, W.: Rev. neurol. **31**:485, 1924.
45. Rülf: Arch. f. Psychiat. **52**:748, 1913; Ztschr. f. d. ges. Neurol. u. Psychiat. **35**:412, 1916.
46. Penfield, W.: Diencephalic Autonomic Epilepsy, Arch. Neurol. & Psychiat. **22**:358 (Aug.) 1929.
47. Hunt, J. R.: Rev. neurol. **2**:201, 1924.
48. Abadie, J.: Rev. neurol. **1**:1201 and 1257, 1932.
49. Klessens, J. J. H. M.: Maandschr. u. kindergeneesk. **3**:307 (May) 1934.

## LISSAUER'S DEMENTIA PARALYTICA

A STUDY OF ITS PATHOGENESIS

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The atypical form of dementia paralytica described by Lissauer and Storch<sup>1</sup> is characterized by transient apoplectic or epileptic attacks followed by residual focal symptoms to which correspond localized anatomic lesions. Discussions in the literature of the nature of the disorder have centered about the pathogenesis of the specific histologic picture of the lesions, namely, status spongiosus and its tendency to laminar distribution. It is the purpose of this contribution to analyze the pathogenic factors suggested by various other investigators and by a study of four additional cases.

### REVIEW OF THE LITERATURE

Since a comprehensive summary of the literature has been outlined by Merritt and Springlova,<sup>2</sup> only contributions to the pathogenesis will be reviewed.

Status spongiosus may occur in both the gray and the white matter in different diseases of the central nervous system. It is characterized histologically by transformation of the tissue into a honeycombed spongy structure with loss of parenchyma and an imperfect repair by fibrous glia. Frequently it does not affect the entire width of the cortex but follows a laminar distribution. Spielmeyer,<sup>3</sup> who introduced the term, understood by it a severe acute disintegrating process produced by a variety of factors. Lissauer and Storch<sup>1</sup> and Alzheimer<sup>4</sup> regarded its occurrence in dementia paralytica as evidence of an advanced process and considered cortical atrophy as the prerequisite condition for its development. Lissauer and Storch<sup>1</sup> explained its laminar distribution as a system process affecting layers II and III, but this was rejected

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From the State Psychopathic Hospital.

1. Lissauer, H., and Storch, E.: Ueber einige Fälle atypischer progressiver Paralyse, Monatschr. f. Psychiat. u. Neurol. **9**:401, 1901.

2. Merritt, H. H., and Springlova, M.: Lissauer's Dementia Paralytica, Arch. Neurol. & Psychiat. **27**:987 (May) 1932.

3. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

4. Alzheimer, A.: Histologische Studien zur Differentialdiagnose der progressiven Paralyse, in Nissl, F.: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Jena, Gustav Fischer, 1904, vol. 1.

by Alzheimer,<sup>4</sup> who observed no definite laminar selection. Concerning the primary element involved in status spongiosus, Fischer<sup>5</sup> disputed Tuczek's<sup>6</sup> view of primary myelin degeneration and maintained that the process originates in the ganglion cells and is not necessarily preceded by atrophy. Bielschowsky<sup>7</sup> described such primary lesions in the white matter, which he designated *Markfleckenbildung* and assumed that, whether in gray or in white matter, the process begins in the inter-cellular ground substance. According to him, this process is produced by circulatory disturbances and is a sequence of capillary hyperemia, increased vascular permeability, edema and inflammatory malacia of the tissue. He ascribed the laminar degeneration to mechanical architectural factors in the cortex. Sträussler and Koskinas<sup>8</sup> agreed with Bielschowsky's<sup>7</sup> theory, but in addition emphasized the importance of vascular spasm in Spielmeyer's<sup>9</sup> sense. They based their conclusions on analogous changes resulting from organic vascular conditions such as arteriosclerosis, the laminar distribution being determined by the vaso-architecture of the cortex (Scholz<sup>10</sup>). Merritt and Springlova<sup>2</sup> maintained that such functional disturbance of the circulation is the only pathogenic factor.

As a result of these differing pathogenic views, the nature of Lissauer's<sup>1</sup> dementia paralytica has been variously interpreted. It was considered as either a direct expression of the process of dementia paralytica itself (Lissauer<sup>1</sup> and Alzheimer<sup>4</sup>) or as resulting from the operation of an additional factor, namely, toxic (Fischer<sup>5</sup>) or vascular (Bielschowsky,<sup>7</sup> Sträussler and Koskinas<sup>8</sup> and Merritt and Springlova<sup>2</sup>). Most authors agreed that spirochetosis cannot be considered as etiologic in view of the negative findings.

A new approach to an understanding of these phenomena has been formulated recently by Brahmühl<sup>11</sup> in his concepts of hysteresis and

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- 5. Fischer, O.: Der spongiöse Rindenschwund, ein besonderer Destruktionsprozess der Hirnrinde, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **7**:1, 1911.
- 6. Tuczek, F.: Ueber der Anordnung der markhaltigen Nervenfasern in der Grosshirnrinde und über ihr Verhalten bei der Dementia paralytica, *Neurol. Centralbl.* **1**:315 and 337, 1882.
- 7. Bielschowsky, M.: Ueber Markfleckenbildung und spongiösen Schichtenschwund in der Hirnrinde der Paralytiker, *J. f. Psychol. u. Neurol.* **25**:72, 1920.
- 8. Sträussler, E., and Koskinas, G.: Ueber den spongiösen Rindenschwund den Status spongiosus und die laminären Hirnrindenprozesse, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **105**:55, 1926.
- 9. Spielmeyer, W.: Die Pathogenese des epileptischen Krampfes, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **109**:501, 1927.
- 10. Scholz, W.: Zur Frage der schichtformigen Veränderungen der Grosshirnrinde, *Zentralbl. f. d. ges. Neurol. u. Psychiat.* **42**:623, 1926.
- 11. Brahmühl, A.: Kolloidchemische Betrachtungsweise seniler und präsenter Gewebsveränderungen, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **142**:1, 1932; *Synäresis und Entzündung*, *ibid.* **148**:1, 1933.

synäresis. He defined these as changes in the colloidal state of the brain, whereby diminished dispersion through dehydration (hysteresis) or separation into parts of different colloidal content (synäresis) occurs, resulting in condensation phenomena. Morphologically, such precipitation is disclosed in the form of senile plaques, neurofibril changes of the Alzheimer type, inflated nerve cells, argentophilic inclusion bodies, etc., observed in senile and presenile disorders of the brain (Alzheimer's disease, Pick's disease, etc.). These are secondary manifestations of primary synäresis. The latter, though not demonstrable as such, must be inferred from the precipitation phenomena and represents a specific reaction of the cerebral tissue. Status spongiosus is another synäretic manifestation in that it occurs through dehydration, release of originally bound fluid and flooding of the tissue. This results in the characteristic spongy appearance. Braunmühl differentiated this type of status spongiosus associated with chronic atrophic conditions from that in severe disintegrating processes (in Spielmeyer's sense, as already mentioned). By comparison of Lissauer's form of dementia paralytica with Pick's disease, he found striking similarities between the two conditions in the cortical atrophy and its focal distribution, primary demyelinization, status spongiosus, laminar degeneration, inflated ganglion cells and argentophilic inclusion bodies. For this reason he regarded the lesions in Lissauer's form as manifestations of early and intensive synäresis, which is apparently released by the inflammation but is not directly caused by it. He assumed the existence of an endogenous synäretic predisposition of the tissue, possibly hereditary in the same sense as in Pick's disease and other abiotrophic conditions. Braunmühl also explained the alternating attacks and remissions frequently observed in Lissauer's form as due to the intermittent action and relative reversibility of the synäresis. The focal character of the lesions he attributed to local accentuations of the process (*Hysteresetönung*) in much the same way as in Pick's disease.

#### REPORT OF CASES

CASE 1.—*Convulsive attacks most pronounced in the left arm; acute excitement eleven months later; clinically, dementia paralytica, diagnosis substantiated by serologic tests; pathologically, advanced atrophy of the entire right hemisphere with laminar degeneration and status spongiosus.*

*History.*—E. G., a Negro aged 33, was admitted to the hospital on Nov. 25, 1931, with a history of convulsions.<sup>12</sup> The family history was meager. One

12. Dr. G. F. Inch, Superintendent of the Ypsilanti State Hospital, and Dr. R. P. Sheets, Superintendent of the Traverse City State Hospital, cooperated in furnishing the material presented in this paper.

paternal uncle was believed to have been psychotic and another committed suicide. The personal history suggested an epileptoid type of personality. The patient contracted syphilis in 1924, for which he received treatment irregularly. The present illness was characterized by an acute onset in January 1931, with a stuttering speech defect and complaints of numbness of the head, followed by convulsive seizures involving the extremities but most pronounced in the left arm. Eleven months later there was an acute onset of mental excitement.

*Examination.*—Studies were inadequate because of the patient's resistiveness. Neurologically, there were spasticity of the limbs, with impairment of gait, diminished corneal reflexes and incontinence. Mentally, there were excitement, confusion and catalepsy. The Kahn reaction of the blood and of the spinal fluid was 4 plus; the Pandy reaction was 3 plus, and the colloidal gold curve was 555543210. A diagnosis of dementia paralytica was made.

*Course.*—The patient's condition remained essentially the same as on admission. Sudden death occurred on Jan. 14, 1932.

*Gross Postmortem Examination.*—Investigations of the organs of the body gave negative results. The brain weighed 1,140 Gm.; the leptomeninges were markedly thickened, and the basal vessels were delicate. The brain was asymmetrical, the right hemisphere being much the smaller. The atrophy was accentuated in the right occipital lobe, which was the harder. Coronal sections revealed marked atrophy of both the gray and the white matter of the entire right hemisphere and dilatation of the right ventricle. The left hemisphere was moderately atrophic. The ependyma of all the ventricles was granular. The basal ganglia, brain stem, cerebellum and spinal cord were without gross changes.

*Histologic Examination of Right Hemisphere (Nissl's Stain).*—The leptomeninges over the whole right hemisphere showed both fibroblastic thickening and diffuse and perivascular infiltration by lymphocytes and plasma cells. The cortex was markedly atrophic throughout, being reduced by one-third to one-half its normal width. In the atrophic regions an almost complete loss of ganglion cells was evident, those remaining exhibiting Nissl's severe and chronic change. An obvious status spongiosus following a laminar distribution was noted in all areas of the hemisphere. This was most impressive in the area striata (fig. 1), where layers III, IVa and IVb showed a honeycombed and spongy structure. There were only a few ganglion cells and an occasional degenerated plasma cell within the interstices. The septums contained numerous blood vessels and glial elements. Blood vessels exhibiting hyaline degeneration with transformation into reddish purple granules extended across the spongy regions. The other layers were atrophic but revealed no evidence of the spongy structure. They contained numerous fibrous astrocytes and shrunken oligodendroglia cells but only a few rod cells. Frequently, in the deeper layers of the cortex inflated ganglion cells with displaced nuclei and pale homogeneous cytoplasm (*Zellblähungen*) were observed. These failed to disclose argentophilic inclusion bodies when prepared by Braunmühl's<sup>11</sup> method. In all other areas of the hemisphere the status spongiosus affected predominantly layers III, V and VI, occasionally involving the entire width of the cortex. The white matter showed extensive atrophy throughout, with an increase of oligodendroglia cells and astrocytes. In the white matter of the cornu ammonis hyaline degeneration of the blood vessels was also noted. There was little evidence of inflammation in the cortex and white matter and only occasional perivascular infiltration.

Sections stained by Weigert's method revealed advanced demyelinization in both the gray and the white matter of the entire hemisphere. Holzer's stain disclosed pronounced marginal gliosis, dense glial networks about the blood vessels,

large fibrous astrocytes in the spongy areas of the cortex and pronounced gliosis of the white matter. Lipoids were scanty in the cortex, being restricted to the walls of the blood vessels, and in the white matter there were only occasional small areas containing fat-laden gitter cells. Proliferation of the blood vessels and abundant perivascular mesenchymal fibers were disclosed with Perdrau's stain. Only small amounts of iron pigment, restricted to the walls of the blood vessels, were found. Spirochetes were not demonstrated with Jahnel's stain.

Histologic Examination of Left Hemisphere: This presented a typical histologic picture of dementia paralytica and absence of focal lesions. The basal ganglia, brain stem and spinal cord showed similar though milder involvement. The cerebellum on the contralateral side to the cortical atrophy presented rather pronounced degeneration, with areas of lobular sclerosis.

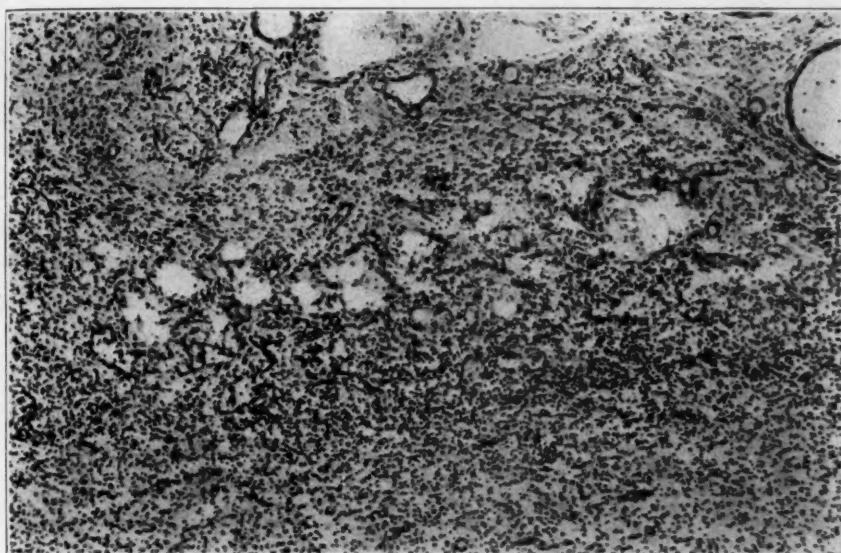


Fig. 1.—A section from the area striata, showing advanced atrophy of the cortex; status spongiosus in layers III, IVa and IVb, and hyaline degeneration of blood vessels. Nissl stain; photomicrograph, Zeiss planar, 20 mm.

*Comment.*—The condition in this case undoubtedly belongs to the group of Lissauer's<sup>1</sup> dementia paralytica because of epileptiform convulsions, predominantly unilateral and antedating the onset of mental deterioration, and the cerebral hemiatrophy. The histologic changes characteristic of laminar status spongiosus were most pronounced in the areas of intense atrophy (area striata). The process, with its advanced gliosis and lack of fresh *Abbau*, was evidently of long standing. The inflammation was characteristically mild, the proliferation of rod cells slight and the iron content scanty. The meninges were considerably thickened, and the marginal gliosis was increased over the atrophic

hemisphere. It is of importance to note the presence of inflated ganglion cells in the cortex and hyaline degeneration of blood vessels in the area striata.

*CASE 2.—Convulsive attacks, often unilateral and followed by transient left hemiplegia and subsequent mental deterioration; clinical diagnosis, dementia paralytica of the tabetic type; pathologically, status spongiosus and laminar degeneration of the entire right temporal lobe, including the island of Reil.*

*History.*—W. V., a white man aged 59, was admitted to the hospital on Jan. 18, 1934, with symptoms of convulsions and mental deterioration. The family history was without significance. He contracted syphilis at the age of 44. Approximately three years prior to admission there developed seizures described as transient periods of dizziness, confusion, visual hallucinations and unconsciousness. Later these were associated with temporary paralysis of the left hand. Shortly before his admission to the hospital the attacks were accompanied by uncontrollable movements of the left arm and leg, and mental decline became apparent.

*Physical Examination.*—There were peripheral arteriosclerosis, mitral stenosis, aortic insufficiency and roentgen evidence of aortic aneurysm. Neurologically, there were Argyll Robertson pupils, impaired hearing, diminished biceps reflexes, absence of patellar and achilles jerks, ataxic gait, incoordination in the finger to nose test, and "a cord type" of bladder function. Mentally, there were euphoria, expansiveness, auditory hallucinations and intellectual deterioration.

*Serologic Tests:* The Kahn reaction of the blood and the spinal fluid was 4 plus; there were 34 cells in the spinal fluid and a colloidal gold curve of 5555554211. A diagnosis of dementia paralytica was made.

*Course.*—In the period of hospitalization the patient had had eight convulsions, accompanied by clonic movements of the left side of the body and unconsciousness and followed by flaccid paralysis of the left side. Two months after admission he became comatose, and death occurred on March 20, 1934.

*Postmortem Examination.*—There were bilateral hypostatic pneumonia, syphilitic aortitis and aneurysm of the ascending aorta, pyelonephritis, chronic cystitis and fatty degeneration of the liver.

The brain weighed 1,134 Gm.; the leptomeninges were thickened, milky and opaque over both convexities, and the basal vessels were moderately sclerosed. The cortex of both hemispheres was atrophic. The atrophy was pronounced in the right temporal lobe, where the gray matter appeared gelatinous and soft and the white matter was greatly reduced. The ventricles were dilated, and the ependyma was granular. The basal ganglia, brain stem and cerebellum showed no gross changes.

Sections stained by Weigert's method revealed advanced demyelinization in the gray and white matter of the entire right temporal lobe (fig. 2). This involved parts of the superior temporal gyrus, the entire middle and inferior temporal gyri and the gyrus fusiformis, amygdaloid nucleus, cornu ammonis, insula and capsula extrema. There was a smaller area of rarefaction in the right frontal lobe.

*Histologic Examination (Nissl's Stain):* In the atrophic right temporal lobe the leptomeninges were markedly thickened, with diffuse and perivascular infiltration by plasma cells and lymphocytes. Some of the meningeal vessels were slightly sclerotic. The cortex was moderately atrophic but extensively degenerated, revealing an obvious status spongiosus. This followed a laminar distribution, regularly involving layer II (fig. 3). In the other layers the process was more irregular,

displaying a tendency to involve layers III, VI, V, I and IV in order of frequency. In the most affected regions the entire width of the cortex was transformed into a spongy structure presenting a moth-eaten appearance and leaving only small preserved islets of nerve cells in layer IV. The few remaining ganglion cells showed Nissl's severe change, but the architecture could still be recognized. Typical inflated cells were frequent in the deeper layers (fig. 4). The cortex was diffusely invaded by numerous *gemästete* glia cells, large fibrous astrocytes, swollen oligodendroglia cells, plasma cells and only occasional rod cells. There were numerous blood vessels in the septums. The white matter was not well demarcated and contained large numbers of proliferated glial elements. In the cornu ammonis the status spongiosus was distributed in a selective manner, affecting the end-plate and Sommer's sector. The inflammation throughout the cortex and the white matter was moderate. With Holzer's stain advanced marginal gliosis,

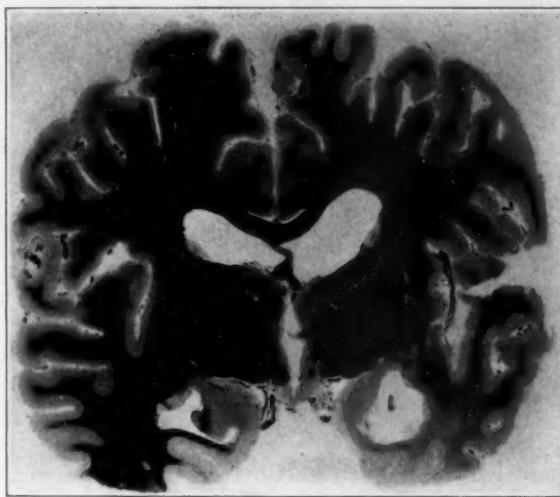


Fig. 2.—Demyelination in the right temporal lobe. Weigert-Kultschitzky stain; reduced by one-half.

a predominance of fibrous astrocytes over glia fibers in the cortex and marked gliosis of the white matter were demonstrated. Perdrau's stain revealed proliferation of blood vessels and perivascular mesenchymal fibers. Scanty amounts of iron pigment were restricted to the walls of the blood vessels and a few microglia cells. Spirochetes were not found. (Because of insufficient material it was not possible to stain for fat or to demonstrate argentophilic inclusion bodies.)

In the remainder of the brain there were moderate histologic findings of dementia paralytica with the exception of pronounced degeneration and gliosis of the pulvinar.

*Comment.*—The condition in this case belongs to Lissauer's<sup>1</sup> group because of convulsive attacks and transient hemiplegia on the left and the localized lesion in the right temporal lobe. The process was in an active phase, the cellular response predominating over fiber production, and

thus the degree of atrophy did not correspond to the severity of the disintegration of tissue. As in case 1, the inflammation was mild and the iron content scanty, but the meninges were markedly thickened and infiltrated and the marginal gliosis was extensive. Inflated cells were frequent. The selective involvement of the cornu ammonis was of interest. The arteriosclerotic changes were mild.

*CASE 3.—Mental deterioration for three years; clinical symptoms and serologic changes of dementia paralytica; seizures, with loss of consciousness, five days before death; patho-anatomically, status spongiosus in the left pallidum and the left temporal lobe.*

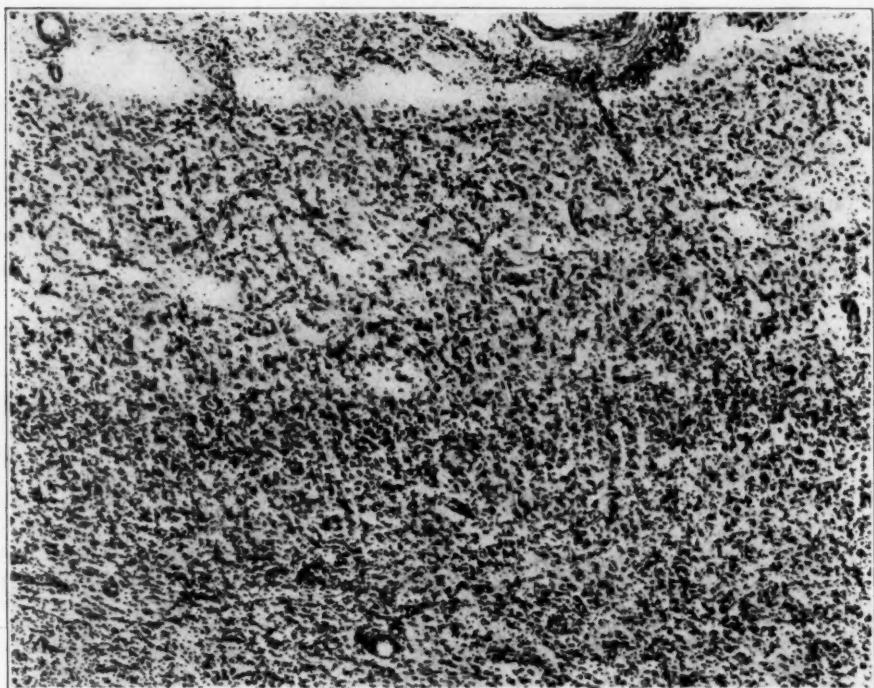


Fig. 3.—Status spongiosus in layers II and III of the cortex in the degenerated temporal lobe. Inflammatory changes in the pia. Nissl stain; photomicrograph, Zeiss planar, 20 mm.

*History.*—N. T., a white man aged 35, was admitted to the hospital on Sept. 5, 1933, with a history of gradual mental deterioration for three years. The family history was not available. There was a history of syphilitic infection. The onset of mental symptoms occurred in 1930, and an acute exacerbation took place just prior to admission.

*Examination.*—Neurologically there were Argyll Robertson pupils, exaggerated deep tendon reflexes and a speech defect of the type observed in dementia paralytica. Mentally there were swings of mood and marked loss of memory, with confabula-

tion. Serologic examination showed a 4 plus Kahn reaction of the blood; the spinal fluid showed a 4 plus Kahn reaction, 11 cells, a 1 plus Pandy reaction and a colloidal gold curve of 5555554210. A diagnosis of dementia paralytica was made.

*Course.*—Therapy with tryparsamide was instituted. Nine days after admission the patient had periods of unconsciousness without convulsive movements and died five days later.

*Postmortem Examination.*—Study of the organs of the body gave negative results. The weight of the brain was not stated; the leptomeninges were thickened; the basal vessels were delicate, and the convolutions were moderately

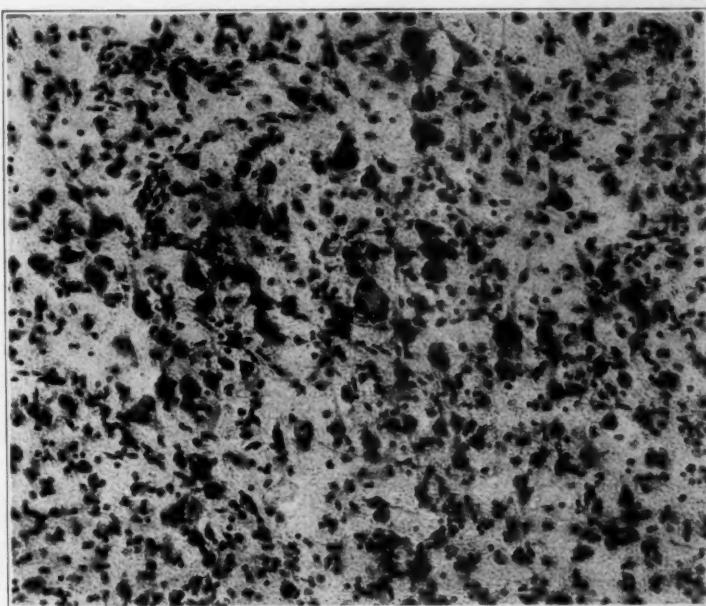


Fig. 4.—An inflated cell is shown in the center of the picture. Nissl stain; photomicrograph, Zeiss objective, 16 mm.

atrophic. On section, the anterior part of the left pallidum revealed marked atrophy and yellowish discoloration. The left ventricle was more dilated than the right.

Sections stained by Weigert's method revealed advanced atrophy, demyelinization and cystic degeneration of the left pallidum and demyelinization of the adjacent inferior fibers of the internal capsule (fig. 5). The left putamen and caudate nuclei were moderately atrophic. In the left temporal lobe the gray and white matter appeared moth eaten (*Markfleckenbildung*).

*Histologic Examination:* In the left pallidum Nissl's stain disclosed extensive gliosis and status spongiosus (fig. 6). The ganglion cells were reduced, those remaining exhibiting severe degeneration, sclerosis, incrustations and calcification. There were numerous closely packed oligodendroglia, microglial and macroglial elements. Holzer's stains demonstrated a dense glial fiber network in the central

part of the pallidum and status spongiosus, rich in large fibrous astrocytes, in its periphery. In the gliosed region, extensive proliferation of blood vessels with perivascular mesenchymal fibers was disclosed with Perdrau's method. There was calcification of the media in some of the blood vessels. The inflammation was mild, but there was a considerable amount of iron pigment in diffuse form in the glia and in the walls of the blood vessels. The lesion was not entirely restricted to the pallidum but affected adjacent portions of the putamen and the internal capsule.

Another area of status spongiosus was present in the cortex of the left temporal lobe, involving parts of the convolutions of the inferior temporal, fusiform and hippocampal gyri. Here, the degeneration followed a laminar distribution, regularly affecting layers II and III, and occasionally layers V and VI, most pronounced in the summits of the convolutions. There was marked loss of nerve cells in the cortex. It contained numerous rod cells, "gemästete" glia and

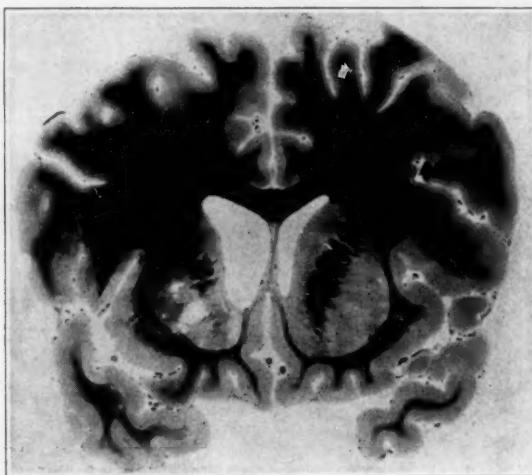


Fig. 5.—Lesion in the left pallidum and adjacent fibers of the internal capsule; moderate atrophy of the corpus striatum; Markfleckenbildung in the left temporal lobe. Weigert-Kultschitzky stain; reduced by one-half.

fibrous astrocytes with little fiber production, causing the gray matter to appear wider than normal. The inflammation in this region was moderate and the iron content was small. (Owing to insufficient material, fat and silver stains could not be done.) Otherwise the brain revealed a mild histologic picture of dementia paralytica.

*Comment.*—Clinically, the condition in this case does not suggest Lissauer's<sup>1</sup> form of dementia paralytica. Anatomically, however, the localized lesion and status spongiosus of the left pallidum correspond with similar cases included in this group by Alzheimer<sup>4</sup> and Jacob.<sup>13</sup>

13. Jacob, A.: *Anatomie und Histologie des Grosshirns*, Leipzig, Franz Deuticke, 1929, vol. 2.

This is further substantiated by similar findings in the left temporal lobe. In this case, again, the inflammation was mild when compared with the severe degenerative condition of the parenchyma.

CASE 4.—*Signs of mental decline for two years before examination; clinical symptoms and serologic changes typical of dementia paralytica; ten days before death, epileptiform seizures followed by coma; pathologically, extensive softening and status spongiosus in the right island of Reil, internal capsule and basal ganglia, corresponding in distribution to the lenticulostriate artery. Disseminated areas of status spongiosus and ischemic foci in the gray matter, "Markfleckenbildung" in the white matter.*

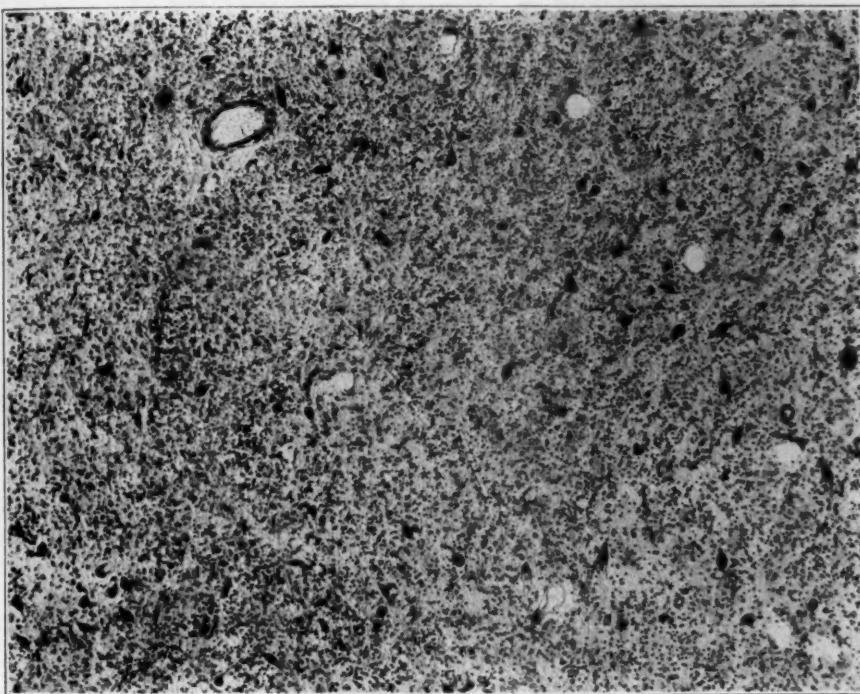


Fig. 6.—Status spongiosus and gliosis of the left pallidum. Nissl stain; photomicrograph, Zeiss planar, 20 mm.

*History.*—F. C., a white man aged 41, was admitted to the hospital on March 24, 1932, with a history of gradual mental decline for two years. The family history was without significance. The patient had contracted syphilis many years before the onset of the psychosis. One month prior to admission there were episodes of marked confusion.

*Examination.*—Neurologically, there were Argyll Robertson pupils, hyperactive deep tendon reflexes and spasticity of gait. Speech and handwriting were typical of dementia paralytica. Mentally there were euphoria, retardation and marked disturbance of memory and intellect.

Serologic Tests: The Kahn reaction of the blood was 4 plus; the spinal fluid showed a 4 plus Kahn reaction, 35 cells, a 3 plus reaction to tests for globulin and a colloidal gold curve of 5555543210. A diagnosis of dementia paralytica was made.

Course.—Tryparsamide was given. Four months after admission epileptiform seizures developed suddenly and the patient died after ten days in coma.

*Postmortem Examination.*—The organs of the body were normal. The brain weighed 1,200 Gm.; the leptomeninges were thickened over both convexities, and the basal vessels were delicate. The convolutions were moderately atrophic, and the right hemisphere was somewhat the smaller. Frontal sections through the right hemisphere revealed softening in the anterior parts of the island of Reil, caudate nucleus, putamen, pallidum and internal capsule. The lateral ventricles were moderately dilated.

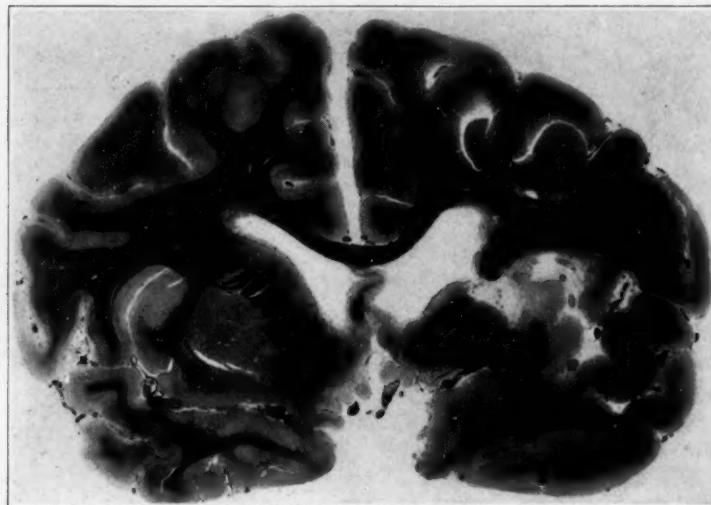


Fig. 7.—Lesion in the territory of the right lenticulostriate artery. Demyelination in the centrum semiovale. Weigert-Kulschitzky stain; reduced by one-third.

Sections stained by Weigert's method demonstrated atrophy and demyelinization of the right insula, more pronounced in its anterior margin and extending into the adjoining rolandic operculum, of the claustrum and of all three capsules (fig. 7). The caudate nucleus and the putamen showed extensive cystic degeneration, and the pallidum was moderately atrophic. There were circumscribed small areas of demyelinization (*Markfleckenbildung*) in the semiovale center and the corona radiata and a moth-eaten appearance of various parts of the cortex. The left hemisphere showed no unusual change.

Histologic Examination: In the right insula the leptomeninges were extensively infiltrated by lymphocytes and plasma cells in both a diffuse and a perivascular manner. Some of the meningeal vessels revealed changes suggesting chronic vascular syphilis. The cortex was reduced to about one-fourth its normal width and showed status spongiosus with pseudolaminar, irregular distri-

bution. In the claustrum, putamen, caudate nucleus, pallidum and capsules a similar status spongiosus prevailed. The parenchyma was almost entirely destroyed, and the cyto-architecture was lost. Only few scattered degenerated ganglion cells remained. There were numerous shrunken oligodendroglia cells, fibrous astrocytes and a few rod cells. Irregularly scattered, but intimately associated with the area of status spongiosus, were simple ischemic foci without reaction, accumulations of microglia cells and organized glial scars, some containing blood pigment. Numerous connective tissue and glial fibers penetrated the spongy areas, giving rise to a complex histologic picture (fig. 8). The inflammatory process throughout was intense. There were only scanty lipoid deposits in the walls of the blood vessels. Iron pigment was present in moderate amounts in the cortex, but in the pallidum and striatum it was increased and occurred both diffusely and in compound granular cells. Spirochetes were not demonstrable.

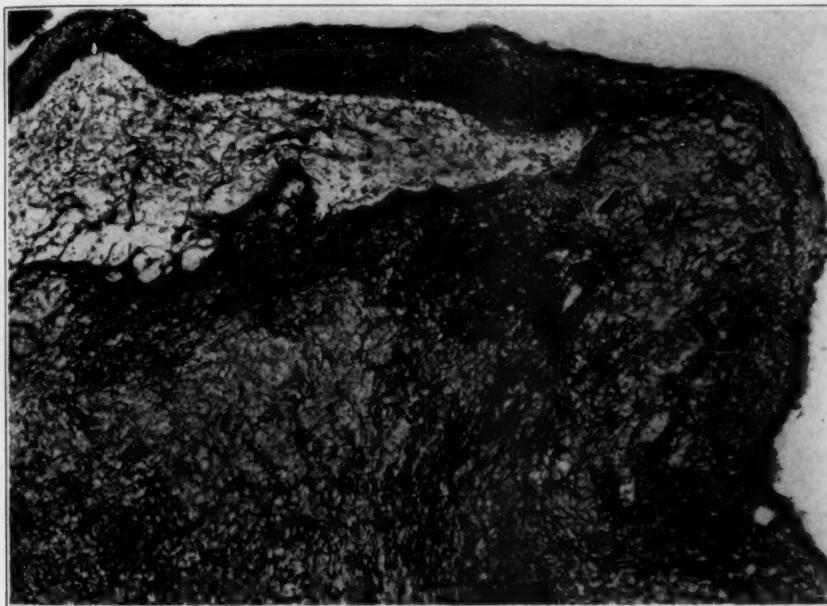


Fig. 8.—Section from the right insula, showing status spongiosus and mixed connective tissue and glia fiber production. Holzer stain; photomicrograph, Zeiss planar, 20 mm.

The same mixed histologic picture of status spongiosus and vascularly determined lesions was disseminated throughout the cerebral gray matter, where it occurred in small foci. The blood vessels in these areas showed only mild inflammation. Otherwise, the usual findings of dementia paralytica were present with the exception of pronounced degeneration and gliosis of the pulvinar.

*Comment.*—Clinically, this patient failed to show definite symptoms of Lissauer's<sup>1</sup> dementia paralytica, but sufficient clinical data were not available. The capsular lesion was vascular, corresponding to the lenticulostriate area of supply, and histologically characterized by marked

connective tissue reaction, intense inflammation, considerable accumulations of iron pigment and foci of ischemic character with an indication of syphilitic vascular involvement. On the other hand, the status spongiosus in the main lesion and in the small foci with *Markfleckbildung* corresponded to Lissauer's<sup>1</sup> form. This case represents a mixed type of dementia paralytica and vascular syphilis classified by Jacob<sup>13</sup> as a form of Lissauer's<sup>1</sup> disease.

#### GENERAL COMMENT

Nissl and Alzheimer<sup>4</sup> established that the parenchymatous degeneration and inflammation in dementia paralytica, though occurring simultaneously, are independent processes. Alzheimer emphasized that the degeneration proceeds along parenchymatous structures and is not produced by involvement of the blood vessels. The truth of such a contention becomes apparent in studies of Lissauer's form of dementia paralytica. In this disorder the inflammatory component is mild and contrasts with the severe involvement of the parenchyma. Perivascular infiltration with plasma cells and lymphocytes is rare in the lesions, being almost entirely limited to the meninges; rod cells are scarce, and the iron content is low. Since this form illustrates a degenerative type of dementia paralytica, its analysis may help to clarify in general the nature of the parenchymatous involvement occurring in this disease.

A departure from the Nissl-Alzheimer approach is evident in the various theories of pathogenesis in which the lesions are ascribed either to organic disease of the blood vessels or to functional circulatory disturbances. On the one hand, such theories disregard the primary degenerative character of the disease process. On the other hand, the proof for an exclusive vascular etiology is inconclusive. Such views as inflammatory malacia (Bielschowsky) and colliquation necrosis (Stengel), to which the status spongiosus is attributed by these authors, fail to take into account the mild inflammation and the different histologic picture of a spongy lesion in contrast to the changes in malacia and necrosis. The analogies drawn between the lesions in Lissauer's form and similar changes occasionally observed in atherosclerotic softenings (Sträussler and Koskinas<sup>8</sup>) are untenable because of the absence in the former of organic vascular pathologic changes. This has led many authors to stress the rôle of functional disturbance of the circulation. Sträussler and Koskinas<sup>8</sup> indicated that interference with the circulation is brought about by the increased thickening of the meninges and marginal gliosis in the lesions, thus producing the status spongiosus. It is known, however, that these are common in dementia paralytica and are merely secondary to the cortical atrophy which they parallel (Alzheimer<sup>4</sup>). Basing their views on Spielmeyer's theory of vasospasms,

Merritt and Springlova<sup>2</sup> arrived at similar conclusions. As evidence for this they pointed to the frequent occurrence of convulsions in the clinical course, the selective involvement of the cornu ammonis and the tendency of the focal lesions to follow a definite vascular pattern of distribution. In the production of convulsive states, however, vasospasms are by no means the only mechanisms responsible (Cobb<sup>14</sup>). With regard to the localization of the lesions, a vascular pattern of distribution does not always occur. Moreover, a similar distribution is observed in Pick's disease, in which there is no reason to assume a vascular relationship. In the four cases here reported, involvement of the cornu ammonis was noted only in case 2 and a vascular pattern of distribution in case 4. The latter case, though atypical, demonstrates the possibility of a vascular pathogenic factor as operating in some instances of Lissauer's form. Its importance, however, has been overemphasized.

Various authors have suggested a toxic etiology of the lesions. Alzheimer<sup>4</sup> assumed it by drawing analogies between the parenchymatous degeneration of dementia paralytica and cases of ergotism and pellagra. Fischer<sup>5</sup> attributed the frequently occurring status spongiosus in Lissauer's form, senile and presenile conditions to a toxic etiology. The argument against such a view, advanced by Merritt and Springlova,<sup>2</sup> was based on the exclusive consideration of the mild inflammation in the lesions, but failed to take into account the severity of the degeneration which may be directly produced by the toxic factor. It is known, for example, that status spongiosus occurs frequently in such toxic-metabolic conditions as Wilson's disease, amaurotic family idiocy and subacute combined degeneration of the spinal cord associated with pernicious anemia. Recently, typical status spongiosus and laminar degeneration were observed in cases of fatal nitrous oxide-oxygen anesthesia<sup>15</sup> and in ergapiol poisoning. In these cases all signs of inflammation were lacking and a direct toxic effect on the cortex was apparent. Such findings suggest the possibility of toxic factors in the etiology of the lesions in Lissauer's form.

In his theories of synäresis, Brahmühl<sup>11</sup> correctly approached the problem by attempting to find an explanation for the parenchymatous degeneration of dementia paralytica. The identical colloidal tissue changes, which he demonstrated as underlying the parenchymatous involvement in this disorder as well as in a variety of atrophic conditions, offer an adequate explanation for the histogenesis of the lesions.

14. Cobb, S.: Causes of Epilepsy, Arch. Neurol. & Psychiat. **27**:1245 (May) 1932.

15. Lowenberg, K.; Waggoner, R., and Zbinden, T.: Destruction of the Cerebral Cortex Following Nitrous Oxide Oxygen Anesthesia, Ann. Surg. **104**:801, 1936.

in Lissauer's form. Thus, the occurrence in the latter of status spongiosus and its origin in the ground substance, the accompanying inflated nerve cells and argentophilic inclusion bodies, etc., justify his assumption of dehydration and condensation phenomena. Similar findings have been observed in the present series of cases (status spongiosus and inflated cells). It is also possible that the hyaline degeneration of the blood vessels, observed in the lesions in case 1, which has been assumed to represent a form of coagulation necrosis, may similarly represent a manifestation of synäresis. Thus, in all probability, colloidal tissue changes can be assumed as underlying the parenchymatous involvement of this disorder.

Braunmühl's assumption of an endogenous synäretic predisposition of the tissue in Lissauer's form seems unwarranted in the present state of knowledge. He arrived at such conclusions from comparisons with chronic atrophic conditions, such as Pick's disease. For this reason, he differentiated between the status spongiosus as it occurs in these atrophic conditions and that described by Spielmeyer in acute severe disintegrating processes. Such a subdivision seems arbitrary. The identical histologic picture of status spongiosus in acute toxic conditions and in metabolic disorders would imply the operation of the same synäretic mechanisms. Such exogenous factors are sufficient to explain the histologic changes by their direct action on the colloidal system, making it unnecessary to postulate an endogenous predisposition.

Braunmühl concluded that in Lissauer's dementia paralytica an endogenous synäretic process is released by the inflammation. On the basis of the preceding discussion it is likely that a variety of direct exogenous factors, namely, toxic, metabolic, inflammatory, vascular and possibly others as yet unknown, are responsible for producing the colloidal changes underlying the lesions of Lissauer's dementia paralytica.

#### SUMMARY

Four cases of Lissauer's dementia paralytica are described, with clinical and pathologic reports.

It is concluded that the colloidal (synäretic) changes underlying the lesions may be directly produced by a variety of exogenous etiologic factors, such as toxic, metabolic, inflammatory and vascular.

## COMBINED SYSTEM DISEASE IN TABES DORSALIS

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The clinical manifestations and pathologic observations in tabes dorsalis are too well known to be discussed in this presentation. A combined lesion of the posterior columns and pyramidal tracts, giving the cord the appearance of subacute combined degeneration, although described, is less frequently observed. The pathologic lesions in a number of cases described in the literature as instances of tabes in combination with involvement of the lateral tracts were due to syphilitic or arteriosclerotic vascular disease, to inflammatory or other diseases of the spinal cord or to descending degeneration from lesions above the spinal cord. A careful survey of the clinical features shows that many are not clearcut cases of tabes. The question arises whether the pathologic changes in the pyramidal pathways can be attributed to the same process that causes the destruction of the posterior columns. In five of a series of fifteen cases of tabes dorsalis in which autopsy was performed there was involvement of the posterior columns and lateral pyramidal tracts. The involvement of these two systems was not caused by syphilitic vascular or inflammatory disease of the cord, nor was the degeneration of the pyramidal tracts the result of lesions above the cord.

### REPORT OF CASES

CASE 1.—C. R., a woman aged 29, who was admitted to the Montefiore Hospital on Jan. 17, 1901, gave a history of limping, weakness and "shaking" of the right leg since 1899. In October 1900 diplopia, mental confusion, loss of speech and right hemiplegia developed. The patient never lost consciousness and, except for involuntary twitchings at night and a slow, monotonous speech, made an uneventful recovery. The patient married at the age of 24. She gave a history of vulvar chancre at an unknown date. The first pregnancy ended in a miscarriage, after which she had headaches for a week and a facial rash. During the second pregnancy, which was normal, she received antisyphilitic treatment. The child who was the result of this pregnancy died at the age of 16 years of "flu."

*Neurologic Examination.*—There were coarse tremor of both upper extremities, with weakness and hypertonus of the right lower extremity; bilaterally hyperac-

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Read before the New York Neurological Society, Dec. 3, 1935.

From the Neurological Division and Neuropathological Laboratory of the Montefiore Hospital.

tive deep reflexes, more on the right than on the left; no abdominal reflexes on the right; bilateral ankle clonus, more on the right than on the left; a Babinski sign on the right; diminished pain sensibility in the lower extremities; normal pupils; moderate optic neuritis; rotatory nystagmoid jerks on lateral gaze; weakness of the right external rectus muscle; weakness of the right side of the face, which was more marked on mimetic innervation, and emotional instability.

*Course.*—The patient contracted a gonorrhreal infection in 1904. In 1905 urinary retention, diminution in vision and paraplegia in flexion developed. The pupils at that time were unequal, the left being larger than the right, and reacted sluggishly to light but well in accommodation. A Wassermann test of the blood in 1912 was positive on two occasions. Examination in 1921 disclosed a systolic blood pressure of 145 and a diastolic pressure of 85; a slightly enlarged and palpable liver; Charcot joints in the knees and spine; absence of the deep reflexes in the lower extremities; loss of the sense of position and vibration in the lower extremities, and a questionable diminution to pain, touch and temperature sensations below the first lumbar segment; Argyll Robertson pupils, and paleness of the optic nerve heads. Mentally, the patient was well oriented, although remote memory was only fair. Wassermann tests of the blood and spinal fluid in 1932 were negative. The patient died after an attack of bronchopneumonia on March 11, 1934.

*Diagnosis.*—The clinical and anatomic diagnosis was thrombosis of the left lenticulostriate artery, tabes dorsalis and lobar pneumonia.

*Gross Postmortem Examination.*—Brain: The meninges were slightly thickened. The vessels at the base showed atheromatous plaques. The left neostriatum was markedly shrunken, and there was dilatation of the left lateral ventricle. An area of softening destroyed the left putamen and part of the capsular fibers.

Spinal Cord: The spinal cord was markedly shrunken. There was translucency of the posterolateral columns in the cervical region.

*Microscopic Postmortem Examination.*—Brain: The superior part of the left internal capsule was shrunken and contained numerous amyloid bodies. In the left putamen and caudate nucleus proliferation of the small capillaries and destruction of the small and large ganglion cells were noted. There was no evidence of perivascular infiltration or of an inflammatory reaction. Sections through the peduncles and pons showed descending degeneration of the left pyramidal fibers.

Spinal Cord: The fasciculus gracilis, the fasciculus cuneatus and the lateral pyramidal tracts of all segments of the cord were demyelinated (fig. 1). In all segments the fasciculus cuneatus was less involved than the fasciculus gracilis. In the cervical region the demyelination of the posterior columns was limited to the fasciculus gracilis (fig. 1A and B); in the uppermost cervical segments the demyelination of the lateral pyramidal tracts was not marked (fig. 1A). The dorsolateral fasciculus (Lissauer's zone), the entrance root fibers and part of the posterior roots also were demyelinated. The dorsal and ventral spinocerebellar tracts and the anterior pyramidal tracts were slightly involved. The myelin sheaths and axis-cylinders were completely destroyed in the central portions of the affected pathways; toward the periphery the myelin and axis-cylinders showed various types of destruction. In Holzer preparations the posterior columns, especially the fasciculus gracilis and the lateral pyramidal tracts, were the seat of a gliotic process. In Sudan III preparations, some of the areas of destruction were filled with fat. The vessels throughout the cord were normal, except for

the small vessels within the anterior fissure, which showed slight proliferation of the intima and hyalinization. The meninges and the cells of the anterior horns disclosed no pathologic changes. There was no inflammatory reaction.

*Comment.*—This patient had thrombosis of the left lenticulostriate artery in 1900, resulting in hemiplegia. The tremor and the signs of involvement of the right pyramidal tract which were present before the onset of tabes (1905) were due to the process in the left caudate nucleus, putamen and internal capsule. Part of the degeneration of the right pyramidal tract in the spinal cord undoubtedly was of a descending type and was caused by the left capsular lesion. This lesion, however, could not explain the degeneration in the left pyramidal tract. Despite bilateral degeneration of the pyramidal tracts, the deep reflexes

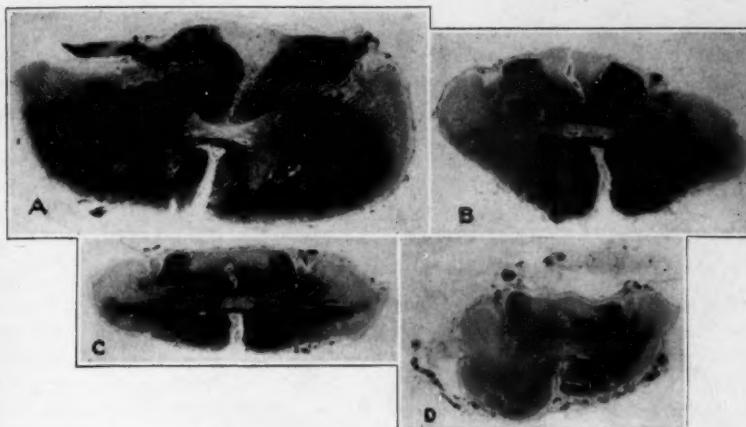


Fig. 1 (case 1).—Transverse sections of the spinal cord showing degeneration of the posterior columns and lateral pyramidal tracts. In the cervical region the demyelination of the posterior columns was limited to the fasciculus gracilis (A and B). In the uppermost cervical segments the demyelination of the lateral pyramidal tracts was not marked (C). Myelin sheath preparation.

of the lower extremities disappeared after the onset of tabes. A number of observers have noted that when tabes follows a primary capsular or cortical lesion, with destruction of the pyramidal pathways, the pyramidal tract signs disappear. The Argyll Robertson pupils, the absence of deep reflexes in the lower extremities, the Charcot disease of the knees and spine and the pathologic process noted in the posterior columns are conclusive evidence that this was a case of tabes dorsalis superimposed on an antecedent lesion of the left capsule. The associated degeneration of the crossed pyramidal tracts in the spinal cord, extending from the upper cervical to the sacral region, and the similarity of the histopathologic changes in the two fiber systems are further

proof that this process in these two systems, except for the right pyramidal tract, which was degenerated at higher levels, was caused by the same pathologic factor.

CASE 2.—M. N., a man aged 43, was admitted to the Montefiore Hospital on Dec. 18, 1905. He gave a history of diarrhea, vomiting and severe epigastric pain in 1899. In 1901 he became constipated and experienced lightning pains in the legs. Unsteadiness in gait and urinary frequency developed in 1904. He had a penile chancre at 35, for which he received antisiphilitic treatment. After this he married. His wife had three children and had no miscarriages.

*Physical Examination.*—Except for a scar on the corona of the penis, examination revealed no abnormality.

*Neurologic Examination.*—There were a Romberg sign, ataxia in the upper and lower extremities, exaggeration of the cremasteric reflexes, a loss of vibratory sensation in the lower extremities and Argyll Robertson pupils.

*Course.*—Laryngeal and gastric crises appeared; these and the pains in the legs became worse. In 1916 the pupils were irregular, unequal and fixed to light and in accommodation. The left superior rectus and the left superior oblique muscle were paretic. Atrophy of the right optic nerve and neuritis of the left optic nerve were present. All the deep reflexes in the lower extremities were absent. Vesical incontinence and constipation were noted. In 1920 bilateral ptosis, perioral and facial tremors, absence of the reflexes in the upper extremities and hyperactivity of the abdominal reflexes were noted. On Aug. 18, 1924, a cerebrovascular insult of bronchopneumonia occurred on the left, from which the patient never fully recovered. He died on Sept. 7, 1924, at the age of 62.

*Laboratory Data.*—The urine contained albumin. The Wassermann reaction of the blood was positive in 1909 and negative after 1914. The Wassermann reaction of the spinal fluid was negative in 1914; the fluid contained 38 cells; six months later and in 1916 the spinal globulin test and the Wassermann reaction of the blood and of the spinal fluid were 3 plus. In 1923 the Wassermann reaction of the spinal fluid became negative; the colloidal gold curve was 0012100000.

*Diagnosis.*—The clinical and anatomic diagnosis was tabes dorsalis, right hemiplegia, siphilitic and atherosclerotic aortitis and bronchopneumonia.

*Gross Postmortem Examination.*—Brain: There was a fresh hemorrhage in the left basal ganglia, and a small amount of unclotted blood was present in the left lateral ventricle. There were no old areas of softening.

Spinal Cord: Transverse sections showed translucency of the posterior columns.

*Microscopic Postmortem Examination.*—Brain: Except for the hemorrhage in the left basal ganglia, sections from various regions of the central nervous system did not show any perivascular infiltrates, inflammatory reaction or other degenerative changes.

Spinal Cord: In myelin sheath preparations the sections in the upper dorsal region showed degeneration of the fasciculus gracilis, the fasciculus cuneatus and the lateral pyramidal tracts (fig. 2). In addition, there was slight degeneration of the dorsal spinocerebellar tracts. The dorsolateral fasciculus (Lissauer's zone), the entrance root fibers and part of the posterior roots were demyelinated. The myelin in these areas disclosed various types of destruction. In Holzer preparations the posterior columns and lateral pyramidal tracts were the seat of a dense

gliotic process. In Sudan III preparations the areas of degeneration in the pathways mentioned were filled with fat-laden cells and free fat. Some axis-cylinders were preserved; others were broken down or showed swelling and corkscrew processes. The pathologic process in the crossed pyramidal tracts differed in no way from that in the posterior columns. In cresyl violet preparations the dura and meninges were thickened but did not contain inflammatory cells. The vessels showed no atherosclerotic changes. The fiber tracts were



Fig. 2 (case 2).—Transverse section of the spinal cord in the upper thoracic region showing degeneration of the posterior columns and lateral pyramidal tracts. Myelin sheath preparation.



Fig. 3 (case 2).—Transverse section of the spinal cord in the midthoracic region showing the degeneration limited to the posterior columns. Myelin sheath preparation.

free from an inflammatory process and the anterior horn cells were normal. The lateral pyramidal tracts below the third dorsal segment were not degenerated (fig. 3). The other fiber tracts at these levels presented the same pathologic changes as did the previous sections. The crossed pyramidal tracts in the cervical segments were not degenerated.

*Comment.*—This patient presented a classic picture of tabes dorsalis complicated three weeks before death by a cerebrovascular insult on

the left. Histopathologically, in addition to the lesion in the posterior column, there was degeneration of both pyramidal tracts in the upper dorsal segments. In the cervical, lower dorsal and lumbosacral regions this process in the pyramidal tracts was absent. The similarity in the finer histopathologic changes in the posterior columns and pyramidal tracts is an indication that this is a result of a single causative agent.

**CASE 3.**—L. B., a man aged 54, was admitted to the Montefiore Hospital on April 10, 1930, with a history of vague gastro-intestinal symptoms in November 1928. The Wassermann reaction of the blood was discovered to be positive, and antisyphilitic treatment was given. Later there appeared diminution of vision, followed by blindness, urinary retention, dysuria and weakness in the lower extremities. The past history, except for an unknown illness when the patient was 24, was without significance. His wife had borne five children, all of whom were living and well, and had no miscarriages.

**Physical Examination.**—The patient was emaciated and bedridden. A tender palpable mass in the left upper quadrant of the abdomen, a draining cystotomy wound and a scar on the dorsum of the penis were noted. The blood pressure was 110 systolic and 70 diastolic.

**Neurologic Examination.**—Slight ataxia in the upper extremities, bilateral dysmetria in the heel to knee tests; equal and active reflexes in the upper extremities and markedly increased reflexes in the lower extremities, with a Babinski sign and confirmatory reflexes; diminished abdominal and cremasteric reflexes; diminution of sensations of pain, temperature and touch over the right first to fifth sacral segments; loss of vibratory sensation from the toes to the hips and impairment of the sense of position in the toes; irregular, unequal pupils, the left being larger than the right and neither reacting to light; bilateral atrophy of the optic nerve and amaurosis; bilateral ptosis, and bilateral diminution of hearing were noted.

**Course.**—The cystitis became worse, and the patient died after an attack of bronchopneumonia on Aug. 31, 1930.

**Laboratory Data.**—Examination of the blood disclosed moderate secondary anemia. The Wassermann reaction of the blood and spinal fluid was four plus. The urine contained albumin and white blood cells. Roentgen examination revealed dilatation, elongation and tortuosity of the ascending limb of the aorta and prominence of the aortic arch.

**Diagnosis.**—The clinical and anatomic diagnosis was tabes dorsalis, pyelonephritis and bronchopneumonia.

**Gross Postmortem Examination.**—**Brain:** The pia-arachnoid was slightly thickened at the base and adherent to the brain tissue. Only the cervical portion of the cord was removed.

**Microscopic Postmortem Examination.**—**Brain:** Except for slight thickening of the pia-arachnoid, which consisted of proliferated arachnoidal cells, there was no pathologic change in the brain. The optic nerve and the chiasm were partly demyelinated and showed destruction of single myelin fibers and axis-cylinders. In the medulla oblongata the ganglion cells of the nucleus gracilis and the nucleus cuneatus disclosed retrograde changes. The pyramids of the medulla oblongata and the internal capsule were normal.

**Spinal Cord:** In the cervical region, near the crossing of the pyramids, there was demyelination of the fasciculus gracilis; the fasciculus cuneatus and fasciculus

interfascicularis (comma tract of Schultze) were spared (fig. 4 A). There were, in addition, partial involvement of the lateral pyramidal tracts and the dorsal and ventral spinocerebellar tracts and slight involvement of the posterior roots and of their entrance zones. In sections through the cervical enlargement the demyelination was more extensive and involved the posterior and lateral columns and the ventral and dorsal spinocerebellar tracts (fig. 4 B). The axis-cylinders were

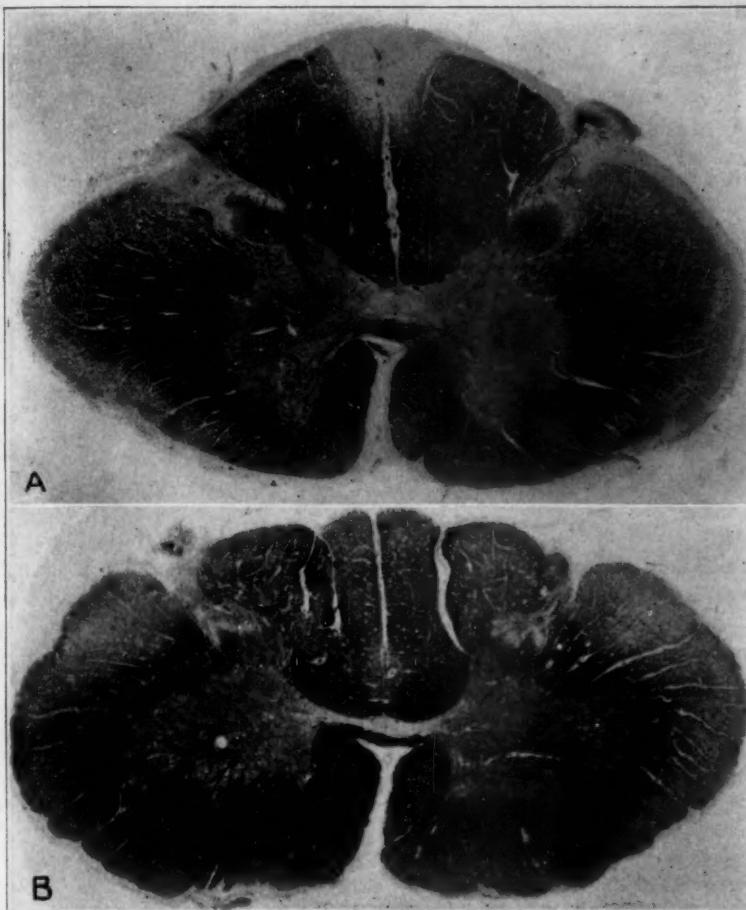


Fig. 4 (case 3).—A, a transverse section slightly below the crossing of the pyramidal tracts showing involvement of the posterior columns (fasciculus gracilis) and crossed pyramidal tracts. Myelin sheath preparation. B, a transverse section of the spinal cord in the cervical region showing degeneration of the posterior and lateral columns, the fasciculus gracilis being more involved than the fasciculus cuneatus. Myelin sheath preparation.

destroyed to a varying degree in the affected zones. The meninges were slightly thickened, the thickening consisting of proliferated arachnoidal cells. There were no inflammatory cells. The blood vessels of the meninges and cord were normal.

There was no disease of the anterior horn cells. None of the involved pathways or roots showed evidences of an inflammatory reaction.

*Comment.*—The clinical course and neurologic symptoms, except for the hyperactive deep reflexes and Babinski sign in the lower extremities, were typical of tabes dorsalis. The pyramidal tract signs were undoubtedly caused by bilateral degeneration of the pyramidal tracts, which was observed only in the cervical region; the rest of the spinal cord was not obtained for autopsy. The absence of degeneration of the pyramidal tracts at higher levels is sufficient proof that this was not a descending degeneration.

CASE 4.—L. B., a man aged 54, was admitted to the Montefiore Hospital on Sept. 4, 1923, complaining of unsteadiness of gait and urinary incontinence. The illness began in 1920, with attacks of severe and constricting pain, radiating from the spine to the scapulae, unsteadiness in gait, ataxia and impotence. In 1922 he experienced "pins and needles" sensations in the feet and numbness in the hands, followed later by urinary incontinence and retention. At this time he received antisyphilitic treatment. He had a penile chancre in 1898 and in 1916 an attack of severe pain in the right upper quadrant of the abdomen associated with diarrhea and vomiting which lasted for five weeks. He married at 24. The wife had six pregnancies, the last two of which resulted in miscarriages. Four children were living and well.

*Physical Examination.*—The patient was anemic and had vesical incontinence and generalized arteriosclerosis. The blood pressure was 124 systolic and 85 diastolic.

*Neurologic Examination.*—There were ataxia in the finger to nose test and marked ataxia in the heel to knee test; diminished deep reflexes in the upper extremities and absence of deep reflexes in the lower extremities; hyperactive abdominal reflexes; wasting of the muscles, with hypotonia; loss of position and joint sensation in the lower extremities; absence of vibratory sensation from the toes to the clavicles; areas of hyperalgesia over the lower dorsal area; pinpoint pupils which were slightly irregular, with no reaction to light but good reaction in accommodation; bilateral ptosis; paralysis of upward gaze, with weakness of the external rectus muscles, and atrophy of the optic nerves.

*Course.*—Antisyphilitic treatment was administered, but the frequency of the abdominal crises and lightning pains in the legs increased. There developed cystitis and terminal bronchopneumonia, and the patient died on Dec. 31, 1927.

*Laboratory Data.*—Examination of the spinal fluid gave negative results until Aug. 8, 1927, when a mastic test gave the curve 3322211000. The Wassermann reaction of the blood and that of the spinal fluid were negative. The urine constantly contained albumin and later red blood cells. A gastric analysis gave normal results and showed free acid.

*Diagnosis.*—The clinical and anatomic diagnosis was tabes dorsalis, pyelonephritis and cystitis and terminal bronchopneumonia.

*Gross Postmortem Examination.*—The brain was normal. The spinal cord showed translucency of the posterior columns.

*Microscopic Postmortem Examination.*—Brain: Sections from various regions of the brain, pons and medulla oblongata did not disclose any degenerative or inflammatory reactions.

Spinal Cord: In the cervical region there was demyelinization of the posterior columns, with greater involvement of the fasciculus gracilis than of the fasciculus

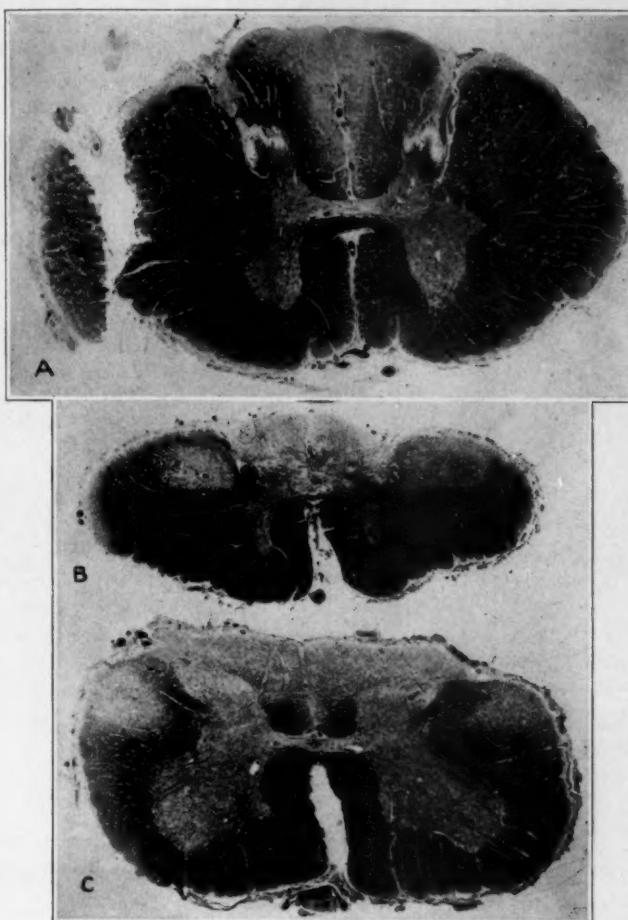


Fig. 5 (case 4).—Transverse sections of the spinal cord from the cervical, dorsal and lumbar regions. In the cervical region the demyelinization was limited to the posterior columns with greater involvement of the fasciculus gracilis than the fasciculus cuneatus (A). In the dorsal and lumbar regions there was involvement of the posterior columns and lateral pyramidal tracts (B and C). Myelin sheath preparation.

cuneatus (fig. 5A). The fasciculus interfascicularis (comma tract of Schultze), the dorsolateral fasciculus (Lissauer's zone) and the entrance root fibers also were degenerated. The posterior roots proper were only slightly involved. The pia-

arachnoid on the posterior surface of the cord was thickened, but there was no evidence of an inflammatory reaction. The vessels of the meninges and cord showed moderate atherosclerotic changes. The anterior horn cells were well preserved. The involved pathways of the spinal cord were not the seat of perivascular infiltrates or of an inflammatory reaction. Transverse sections of the spinal cord from the first thoracic to the sacral segments presented, in addition, degeneration of the lateral pyramidal tracts (fig. 5 *B* and *C*). The dorsal spinocerebellar tracts were not involved. In Holzer preparations there was gliosis of the posterior columns and pyramidal tracts (fig. 6). In sections stained for fat these pathways contained fatty deposits, some of which were gathered in the perivascular spaces. Various degrees of destruction of myelin and axis-cylinders were noted throughout these pathways.

*Comment.*—The neurologic signs and symptoms were classic for tabes dorsalis. Although the Wassermann reactions of the blood and



Fig. 6 (case 4).—Transverse section of the spinal cord showing gliosis of the posterior columns and lateral pyramidal tracts. Holzer stain.

spinal fluid were negative, the mastic curve was indicative of syphilitic infection. The absence of mental symptoms and of perivascular infiltrates in the cortex and the preservation of the arrangement of the cyto-architectural layers are sufficient to exclude a diagnosis of dementia paralytica. The combined degeneration of the crossed pyramidal tracts and posterior columns from the thoracic to the sacral segments and the identical histopathologic process in the two pathways are an indication that there was a common pathogenic factor. In our opinion the slight thickening of the meninges in the cervical region, without any inflammatory reaction, could not have caused this combined degeneration. The absence of degeneration of the pyramidal tracts above the thoracic segments is sufficient indication that their involvement was not due to cerebral disease.

CASE 5.—S. S., a man aged 56, was admitted to the Montefiore Hospital on Dec. 26, 1933, complaining of pains in the chest, joints and legs and intermittent acral paresthesias since 1926. In 1931, after financial reverses, he had a "nervous breakdown" accompanied with coughing and substernal oppression, a sensation of falling while walking, tremor of the legs, shooting pains in the left leg, impairment of hearing and urinary and fecal incontinence. There was a history of penile chancre in 1898, for which he received injections for a period of six months. Marriage at the age of 28 to a woman aged 48 resulted in no pregnancies.

*Physical Examination.*—The patient was pale, thin, chronically ill and bedridden. There were left dorsal scoliosis and lumbar kyphosis, with a gibbus in the upper lumbar region and flaring of the ribs; a scar on the glans penis; vesical incontinence, and a blood pressure of 140 systolic and 80 diastolic.

*Neurologic Examination.*—The patient was mentally dull and apathetic, with poor powers of concentration. There were tremors of the outstretched fingers; ataxia in the lower extremities; localized atrophy in the palms of the hands, with fibrillations between the right thumb and the index finger posteriorly; diminution in the power of the lower extremities; diminished deep reflexes in the upper extremities and absence of reflexes in the left lower extremity; absence of abdominal reflexes on the right, and an Oppenheim sign on the right; diminution of pain and temperature sensations over the fourth lumbar segment on the right, the fifth lumbar segment on the left and bilaterally over all the sacral segments; impairment of the vibration sense and loss of position sense in the small toe of the right foot; irregularity of the pupils, which were fixed to light and in accommodation; narrow palpebral fissures, the left being wider than the right; atrophy of the optic nerves, and bilateral nerve deafness.

*Course.*—The patient received typhoid vaccine, with only temporary relief of pain. Wrist drop developed on the right, with sensory changes along the radial and ulnar distributions. Two days after a cisternal puncture, the patient became stuporous. He died on Nov. 24, 1934, after bronchopneumonia.

*Laboratory Data.*—Examination of the blood showed a very mild secondary anemia and leukocytosis. The Wassermann reaction of the blood was negative, and that of the spinal fluid was four plus. The spinal fluid contained 10 cells and 60 mg. of protein; the mastic curve was 1444210000. The urine contained albumin and casts. Roentgen examination disclosed bony condensation in the lumbar vertebrae, with narrowing of the bodies of the second and third and fusion of the fourth and fifth vertebrae, with marked productive changes along the left half of the second lumbar vertebra.

*Diagnosis.*—The clinical and anatomic diagnosis was tabes dorsalis, subarachnoid hemorrhage and bronchopneumonia.

*Gross Postmortem Examination.*—*Brain:* There was a subarachnoid hemorrhage in the region of the left sylvian fissure and over both frontal convolutions, the temporal poles, the hippocampus and part of the base of the brain. Clotted blood was present in the region of the fourth ventricle.

*Spinal Cord:* A subdural clot was present throughout the extent of the cord. Transverse sections of the cord showed translucency of the posterior columns.

*Microscopic Postmortem Examination.*—*Brain:* Sections of the meninges of the brain disclosed an inflammatory process, moderate endarteritic vessels and a subarachnoid hemorrhage. The arrangement of the cyto-architectural layers was well preserved. Except for a slight perivascular reaction within some of the

vessels of the first cortical zone, due to the meningitis secondary to the subarachnoid hemorrhage, there was no inflammatory process within the other cortical layers.

**Spinal Cord:** In myelin sheath preparations there was degeneration of the fasciculus gracilis and fasciculus cuneatus throughout all segments, the latter being the less involved (fig. 7 *A* to *C*). The dorsolateral fasciculus (Lissauer's zone), the entrance root fibers and the posterior roots also showed destruction of myelin. The spinocerebellar tracts were not involved. In the lumbosacral region, in addition to the preceding, there was degeneration of the right lateral pyramidal tract (fig. 7 *D*). This tract was spared in all other segments. Under higher power, destruction of the myelin fibers and axis-cylinders was the same as in the preceding cases. In cresyl violet preparations the meninges of the cord in the

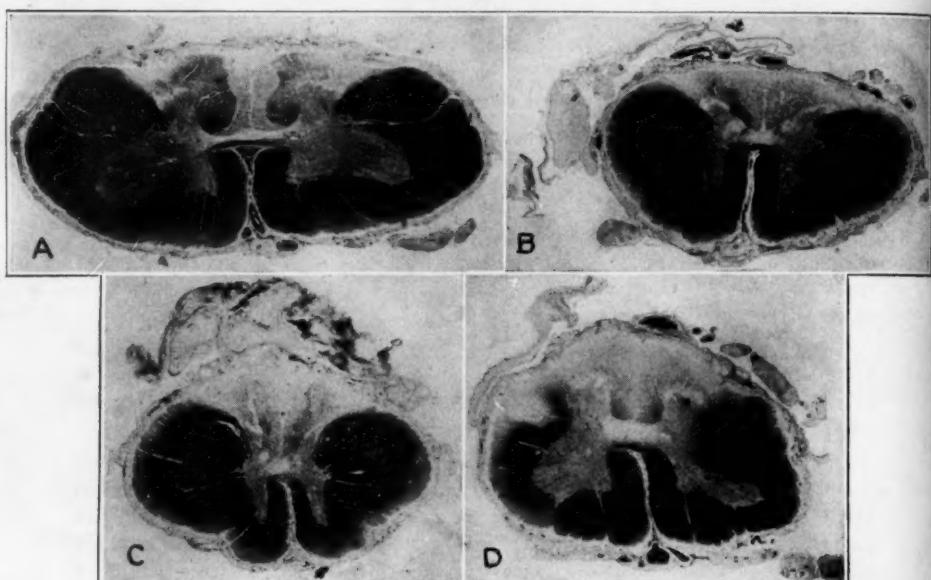


Fig. 7 (case 5).—Transverse sections of the spinal cord. In the cervical region the degeneration is essentially limited to the fasciculus gracilis (*A*). In the thoracic region the demyelination is limited to the posterior columns (*B* and *C*). Notice the thickened meninges in the thoracic region (*C*). In the lumbar region the degeneration destroyed the posterior columns and the right lateral pyramidal tract (*D*). Myelin sheath preparation.

thoracic region were thickened and infiltrated by inflammatory and red blood cells (fig. 7 *D*). Subarachnoid hemorrhages, as in the higher centers, also were noted. A number of the vessels of the spinal cord showed moderate endarteritis, without obliteration of the lumen; this process was less marked in the lumbosacral segments. The anterior horn cells in the cervical enlargement showed pigment atrophy. The involved pathways were not the seat of an inflammatory process.

*Comment.*—Clinically this patient, except for slight mental dulness and apathy, the presence of signs of mild involvement of the right pyramidal tract and the mastic curve suggestive of dementia paralytica, presented a picture of tabes dorsalis. The absence of perivascular infiltrates and of an inflammatory reaction within the cortical areas and the preservation of the arrangement of the cyto-architectural layers are sufficient to rule out a diagnosis of dementia paralytica. The subarachnoid hemorrhage, which was the end-result of the cisternal puncture two days before the patient's death, could not have been the cause of the clinical picture or of the characteristic pathologic picture of tabes dorsalis in the spinal cord. The degeneration of the right lateral pyramidal tract, limited to the lumbosacral region, which accounted for the Oppenheim sign on the right, had the same histopathologic picture as that seen in the posterior columns. The meningitic process in the midthoracic region, an end-result of the subarachnoid hemorrhage, could not be the cause of the lesion of the right crossed pyramidal tract, because this pathway was spared at all levels above the lumbosacral region. We therefore conclude that the lesion of the right pyramidal tract was caused by the same agent which resulted in the destruction of the posterior column.

#### COMMENT

The combination of lesions of the pyramidal tract and posterior column has been described by a number of observers (Westphal,<sup>1</sup> Prevost,<sup>2</sup> Pierret,<sup>3</sup> Schmaus,<sup>4</sup> Raymond,<sup>5</sup> Déjerine,<sup>6</sup> Kattwinkel<sup>7</sup> and others). Some of these were clinical reports, and the cases were placed in this category because of the pyramidal tract signs. These must be discarded, because lesions of the pyramidal tract may have been caused

1. Westphal, C.: Ueber strangförmige Degeneration der Hinterstränge mit gleichzeitiger fleckweiser Degeneration des Rückenmarks, Arch. f. Psychiat. **9**: 389, 1879.

2. Prevost, J. L.: Ataxie locomotrice: Sclérose des cordons postérieurs, compliquée d'une sclérose symétrique des cordons latéraux, Arch. de physiol. norm. et path. **4**:764, 1877.

3. Pierret, M.: Note sur la sclérose des cordons postérieurs dans l'ataxie locomotrice progressive, Arch de physiol. norm. et path. **75**:364, 1871.

4. Schmaus, H.: Zur pathologischen Anatomie der Seitenstrangerkrankung bei Tabes dorsalis, Deutsches Arch. f. klin. Med. **46**:116, 1889-1890.

5. Raymond, F.: Contribution à l'anatomie pathologique du tabes dorsalis: Sur la topographie des lésions spinale du tabes au début, Rev. de méd. **11**:1, 1891.

6. Déjerine, J., and Thomas, A.: Maladie de la moelle épinière, Paris, J.-B. Baillière & fils, 1909.

7. Kattwinkel, W.: Ueber aquirierte kombinierte Strangsclerosen, Deutsches Arch. f. klin. Med. **75**:37, 1902.

by vascular accidents in higher centers, which is not at all uncommon in syphilis of the nervous system. Other instances of this combination may have been due to subacute combined degeneration (pernicious anemia), Friedreich's ataxia, pellagra, carcinomatosis, diabetes, vascular disease of the cord due to arteriosclerosis or syphilis or meningitis of the spinal pia-arachnoid. Keschner and Davison<sup>8</sup> reported a case of vascular disease of the posterolateral spinal arteries due to syphilis in which the pathologic process was limited to the posterolateral columns. Such cases certainly cannot be classified as combined system disease in tabes.

Many of the clinicopathologic reports recorded before the Wassermann test had been devised must be discarded. Kattwinkel reported eight such cases in 1902. A careful analysis of these cases shows that they were not typical of tabes dorsalis. The author admitted that in most of the cases, with the exception of case 2, there were a myelitic process and severe vascular disease of the cord. Even in case 2 he stated that the spinal vessels of the dorsal regions "were markedly sclerotic." In case 1 there was no degeneration of the pyramidal tracts. In cases 3 and 4 there were marked atherosclerotic changes in the vessels. In case 5 there was a syphilitic myelitic process in the fourth thoracic segment. Case 6 was not typical of tabes, and at autopsy there was a cavity in the lumbar enlargement with hyaline degeneration of the small vessels. Cases 7 and 8 were questionable because the author failed to record the pupillary observations. Nothing was mentioned in all these cases about the histopathologic picture in the higher centers. Since Kattwinkel's report there has been, as far as we know, no recorded clinicopathologic study of combined system disease in tabes.

Marie and Crouzon<sup>9</sup> found four instances of combined tabes among fifty-five patients observed clinically, and Bramwell<sup>10</sup> found five in forty-seven cases. Seven of a series of one hundred and sixty-six patients with tabes admitted to the Montefiore Hospital since 1914 showed pyramidal tract signs. Fifteen of these patients came to necropsy, and in five there was also degeneration of the pyramidal tracts. Pyramidal tract signs, however, were found only in cases 3 and 5. In case 3 bilateral degeneration of the pyramidal tracts was

8. Keschner, M., and Davison, C.: Myelitic and Myelopathic Lesions: III. Arteriosclerotic and Arteritic Myelopathy, *Arch. Neurol. & Psychiat.* **29**:702 (April) 1933.

9. Marie, P., and Crouzon, O.: Étude clinique de la forme tabétique des scléroses combinées, *Rev. neurol.* **11**:326, 1903.

10. Bramwell, B.: Analysis of One Hundred and Fifty-Five Cases of Tabes, *Brain* **25**:19, 1902.

observed only in the cervical region, since the rest of the cord was not obtained for autopsy. In case 5 there was only an Oppenheim sign on the right; histopathologically, only the right pyramidal tract in the lumbosacral region was degenerated. In spite of the marked degeneration of the pyramidal tracts in cases 2 and 4, the deep reflexes were absent. Of interest is case 1, in which hemiplegia occurred about five years before the onset of tabes. The patient was under constant observation. The pyramidal tract signs on the right side caused by thrombosis of the left lenticulostriate artery disappeared after the onset of tabes. It has been noted that if hemiplegia precedes the onset of tabes the pyramidal tract signs may disappear; if it follows tabes, the deep reflexes on the hemiplegic side, which were absent, may become hyperactive. The pathologic condition most likely accountable for the paraplegia in flexion in case 1 was the bilateral degeneration of the pyramidal tracts in the spinal cord. A bilateral lesion of the pyramidal tracts in higher centers also may produce paraplegia in flexion; this, however, was not the case in our patient. Clinically, all our patients presented a clearcut picture of tabes dorsalis. In addition, all except the fourth patient showed a positive Wassermann reaction, and in this case the colloidal gold curve was suggestive of dementia paralytica. In case 5 the slight mental dulness, the apathy and the mastic curve suggested the possibility of a diagnosis of dementia paralytica. The preservation of the normal arrangement of the cyto-architectural layers and the absence of any perivascular infiltrates or of an inflammatory reaction within the cortical zones are sufficient to eliminate a diagnosis of dementia paralytica.

It is to be emphasized that the finer histologic picture in the pyramidal tracts, such as destruction of the myelin sheaths and axis-cylinders and the gliotic process, was similar to that in the posterior columns. On this basis and because in every one of our cases the sections made above the spinal cord showed no evidences of disease of the pyramidal tracts, except in case 1, in which there was a preexisting vascular insult, we believe that the lesion in the pyramidal tracts in the cord was caused by the same agent that produced the destruction of the posterior columns. With the exception of case 5, in which there was pigment atrophy, the anterior horn cells in the entire group were well preserved.

The question arises whether there is a common pathogenic factor for the causation of the combined degeneration of the posterior columns and the pyramidal tracts. The pathogenesis of tabes, as is well known, is still a moot question. It is therefore necessary briefly to discuss and consider the theories concerned.

According to Marie and Guillain,<sup>11</sup> the initial lesion in tabes dorsalis is syphilitic infection of the lymphatic system of the posterior surface of the cord and of the corresponding meninges. The involvement of the posterior columns in tabes is caused by the disease of the lymphatic channels in the pia-arachnoid and in the intramedullary septums. The lesion of the posterior roots is secondary to the involvement of the lymphatic system on the posterior surface of the cord.

Obersteiner and Redlich<sup>12</sup> stated that the degeneration of the posterior columns is caused by an inflammation of the pia-arachnoid or some other pathologic process which produces strangulation of the posterior roots at their entrance zone into the cord as they pass through the pia-arachnoid. Nageotte<sup>13</sup> agreed with this theory, except that he stated that the strangulation is in the radicular nerve in front of the spinal ganglia. Hassin<sup>14</sup> stated that the pathologic changes taking place in the meninges and their spaces are responsible for the changes in the spinal cord. The inflammatory process in the dura and the pia-arachnoid obstructs the perineural spaces, thus interfering with the flow of the cerebrospinal fluid from the subarachnoid space. The stasis of this fluid results in the pathologic changes seen in the spinal cord.

Some observers believe that lesions in the peripheral nerves may lead to involvement of the posterior root ganglia and even of the posterior roots and columns. Although changes in the peripheral nerves have been found in tabes dorsalis, few observers believe the changes in the posterior columns can be explained on this basis.

Strümpell<sup>15</sup> and later Spielmeyer<sup>16</sup> regarded the pathologic process in tabes dorsalis as a selective primary degeneration of certain tracts and not as the end-result of an inflammatory process of the meninges or a constriction of the posterior roots or of the radicular nerves. Tabes dorsalis is, then, the end-result of an endogenous toxin which attacks simultaneously the posterior columns and the roots. It is a system

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11. Marie, P., and Guillain, G.: Les lésions du système lymphatique postérieur de la moelle sont l'origine du processus anatomo-pathologique du tabes, Rev. neurol. **11**:49, 1903.
12. Obersteiner, H., and Redlich, E.: Ueber das Wesen und Pathogenese der tabischen Hinterstranges-Degeneration, Arb. a. d. Inst. f. Anat. u. Physiol. d. Centralnervensyst. an d. Wien. Univ. **2**:158, 1894; **3**:192, 1895.
13. Nageotte, I.: Pathogénie du tabes dorsal, Paris, G. Naud, 1904.
14. Hassin, G. B.: Tabes Dorsalis, Arch. Neurol. & Psychiat. **21**:311 (Feb.) 1929.
15. Strümpell, A.: Die pathologische Anatomie der Tabes, Arch. f. Psychiat. **12**:723, 1882.
16. Spielmeyer, W.: Pathogenese der Tabes und Unterschiede der Degenerationsvorgänge im peripheren und zentralen Nervensystem, Ztschr. f. d. ges. Neurol. u. Psychiat. **91**:627, 1924.

disease, like amyotrophic lateral sclerosis, subacute combined degeneration, Friedreich's ataxia and others. Spielmeyer, experimenting with a spinal anesthetic, such as stovain (benzoyldimethylamino-ethylpropanol), produced, when using only small quantities, degeneration of the posterior roots and posterior columns.

Marie and Guillain's theory has been disproved, for in many cases of tabes the inflammatory reaction of the meninges cannot be demonstrated. The lymphatic system, which is not present in the brain and cord but which can be compared to the perivascular system, in most cases of tabes, does not show any perivascular infiltration.

The theories of Obersteiner and Redlich, Nageotte and Hassin, while they may explain the pathogenesis in some cases of tabes, do not satisfactorily explain it in most of them. Meningitis is frequently absent in tabes; when it is present it is not sufficient to produce strangulation of the posterior roots or of the radicular nerve or obstruction of the perineurial spaces, with ensuing stasis of the cerebrospinal fluid resulting in degeneration of the spinal cord. This theory certainly does not explain the pathologic process in the posterior columns and pyramidal tracts observed in our cases and others reported in the literature, as well as the occasional involvement of the cranial nerves in tabes. Furthermore, in interstitial inflammatory conditions of the posterior roots and their course through the pia mater and in many cases of severe meningitis of the posterior surface of the cord, degeneration of either the roots or the posterior columns may be absent. This can be said also of many instances in which the subarachnoid spaces of the spinal cord are obstructed by neoplasms, abscesses, inflammatory conditions of the meninges or thickening of the dura and meninges from other causes. In our opinion, the only plausible explanation for the pathologic changes in many cases of tabes dorsalis is the liberation of toxic substances which act specifically on the posterior roots and posterior columns. At times this toxin may act also on other pathways and, as in our cases, on the lateral pyramidal tracts. This is the only theory which can explain the simultaneous involvement of the posterior columns and lateral pyramidal tracts in our cases.

As is well known, the lesion in tabes is more commonly observed in the lower dorsal and lumbosacral segments. The degeneration of the fasciculus gracilis seen in the upper dorsal and cervical regions is an ascending degeneration. Occasionally the fasciculus cuneatus also may be involved in the cervical region, as occurred in some of our cases. Why the same toxin should act most frequently on the enumerated pathways in the lower dorsal and lumbosacral segments is difficult to explain. The exact nature of the toxin which causes this

process has not so far been demonstrated. For this reason our assumption is still hypothetic.

#### CONCLUSIONS

Five of fifteen patients with tabes dorsalis who came to necropsy showed combined degeneration of the posterior columns and lateral pyramidal tracts. Clinically, two of these had presented signs of involvement of the pyramidal tracts. In a series of one hundred and sixty-six patients with tabes dorsalis observed clinically, including the fifteen mentioned, seven presented pyramidal tract signs.

The various theories of tabes dorsalis are reviewed, and the most plausible explanation for the changes in our patients is the direct action of toxic substances on the posterior columns and lateral pyramidal tracts.

#### DISCUSSION

DR. BERNARD SACHS: I am sorry that I did not know I might be called on to discuss this subject, as it would have been of interest to look up old records. The presentation is of extreme interest, and there is always the question of what is called tabes pathologically and what clinically. I can say only that cases are not infrequent in which the diagnosis of typical tabes is made and then in the course of the disease symptoms develop that are attributed to involvement of the pyramidal tract. I recall a number of such cases at a time when I was particularly interested in the pathologic changes in cerebrospinal syphilis. While the theory may be correct that a toxin produces posterior sclerosis and perhaps also a change in the pyramidal tract, it is a mistake to suppose that the pathologic picture is necessarily identical in all cases of tabes. I do not believe that it is. I believe that in many cases the posterior sclerosis may be a primary degeneration. I grant that in some instances it may be due to a special toxin, but in the cases in which I made an examination it was evident that the process started in the peripheral portion of the spinal cord. If one examines many sections one sees actual constriction of the nerve strands as they enter the posterior column, with a considerable amount of exudate and marked chronic leptomeningitis and pachymeningitis at various levels. I am sorry that the blood vessels were not included in most of the sections that have been shown. That is a mistake often made in the preparation of sections of the spinal cord. The importance of the vessels of the spinal cord is neglected. In many cases one would obtain positive evidence of syphilitic endarteritis. I am willing to agree with the interpretation given in the various cases, but I believe that the syphilitic process in the peripheral portion of the cord is largely responsible for the development of the lesions in many instances. In cases in which typical symptoms of involvement of the posterior column and pyramidal tract were shown, I believe that a degenerative process occurred in the pyramidal tract, in addition to the posterior sclerosis. Let it be granted also that there may be a gradual invasion from the periphery into the lateral region of the pyramidal tract and that in this way the symptoms one ordinarily attributes to involvement of the pyramidal tract are brought about.

DR. FOSTER KENNEDY: I cannot agree with Dr. Davison and Dr. Kelman when they maintain that the only explanation for the concomitant degeneration of the pyramidal tracts is that of a specific toxin. It has been clear to most observers who have examined specimens and sections of the cord that in many instances pachymeningitis caused degeneration of the pyramidal tract by pressure. If Dr. Davison will look through the volumes of *Brain* for 1908 and 1909 he will find a number of studies dealing not only with these changes in the pyramidal tract but with typical syringomyelic lesions produced by pachymeningitis associated with tabes.

DR. E. D. FRIEDMAN: May I ask whether there was evidence of primary or severe secondary anemia in any case? I ask this question because some of my colleagues may remember a patient whom we had an opportunity to observe at the Mount Sinai Hospital, in the service of Dr. Sachs, in whose illness the sequence was as follow: syphilis, followed by tabes; later, development of a blood picture which was similar to that of pernicious anemia, and, finally, development of the symptom complex characteristic of combined sclerosis. I wish to ask whether in any case reported here there was anything which simulated this syndrome.

DR. S. P. GOODHART: While the authors of the paper have given a convincing pathologic demonstration of the occasional occurrence of degeneration of the pyramidal tract in cases of tabes, their assumption of a specific toxin is not tenable. A specific toxin should, as I see it, be present far more frequently, so that pyramidal involvement would be the rule rather than the exception, since syphilis would certainly be accompanied with constant specific toxins. If the long held theory referred to by Dr. Sachs is correct, i. e., that there is extension to the posterior column from the posterior root, involvement of the motor tracts is indeed difficult to explain except as an independent process.

DR. HAROLD KELMAN: In reply to Dr. Sachs, particular emphasis was laid on the blood vessels; they were carefully examined, and there was no evidence of syphilitic endarteritis or of arteriosclerotic change. The degeneration of the fiber tracts in the cases of tabes is best explained on a toxic basis, although in some cases reported in the literature other factors may have played a rôle. A great many more sections were made than could be shown here.

With regard to what Dr. Kennedy said, the same principle applies to pachymeningitis. The slight meningitis encountered in some of the fifteen cases in which examination was made was not severe enough to cause degeneration of the posterior root and posterior column. Although degeneration of the posterior column was marked, little demyelinization was noted in most of the posterior roots.

In reply to Dr. Friedman, gastric analysis was made and free acid was found to be present in two cases. Mild secondary anemia was observed in two cases, in neither of which the picture suggested pernicious anemia. The pathologic process in these cases is different from that in subacute combined degeneration. In the latter one finds the characteristic honeycomb appearance and patchy areas of demyelinization, which are not present in tabes. The gliosis which is evident in these cases is more marked than in subacute degeneration (except in cases of the latter condition in which treatment has been given, as shown by Dr. Davison).

## UNSTEADINESS OF THE HEART RATE IN PSYCHOTIC AND NEUROTIC STATES

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We report here some results of studies on the heart rate which were begun several years ago. In previous reports<sup>1</sup> the cardiochronograph has been described, and the methods of study have been discussed. A general tendency in our results which seemed particularly interesting and significant was the relative steadiness of the heart rate in psychotic patients during periods of apparent emotional experience, as compared with the fluctuations of heart rate in normal persons when emotionally disturbed. The possible significance of this observation and its bearing on the inner affective experience of the psychotic patient have been touched on in previous publications and have been a topic of continuous interest during further studies.

As a matter of personal experience for the investigator, the observation of the heart record as it actually registers during the course of an interview gives an opportunity to compare and contrast the subject's overt expression of emotional disturbance with what is happening to the heart rate. When one wishes, however, to summarize and discuss such observations with others, as in this communication, there are considerable difficulties. The course of a dozen personal conversations cannot be reduced to any mathematical expression or common denominator. Even the heart record is so continuously and variably variable that one finds difficulty in stating with satisfactory clarity the type of degree of unsteadiness. The difficulty in talking about the matter is increased by

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1. Whitehorn, J. C.; Kaufman, M. R., and Thomas, J. M.: Experimental Study of Heart Rate in Relation to Emotion, *Arch. Neurol. & Psychiat.* **30**:950 (Oct.) 1933; papers read before the Massachusetts Psychiatric Society, Dec. 14, 1934; Heart Rate in Relation to Emotional Disturbances, *Arch. Neurol. & Psychiat.* **33**:712 (April) 1935.

the fact that few physicians have a realization of the normal expectancy. Most finer instrumental studies of the heart's regularity have been made by the electrocardiogram, and that type of record spreads the beat to beat variability in horizontal sequences so far apart that only gross differences are noted. Even a cardiologist, looking at a cardio-chronographic record for the first time, may have some hesitation in believing the variability shown.

In this report we shall present two modes of representing the unsteadiness of heart rate in order to facilitate discussion. First, however, it will be helpful to illustrate by example the kind of raw material which we are trying to condense into understandable general terms.

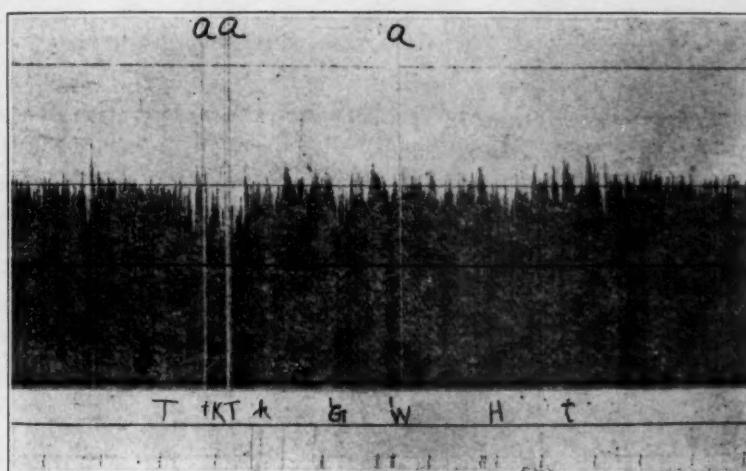


Chart 1.—Portion of a record of a personal interview, described in the text. *a* represents artefacts.

Chart 1 is a portion of a record from an experiment on a 40 year old psychotic patient at the McLean Hospital, with a mild but long-lasting depressive reaction.

The subject had been lying quietly on a couch alone in the room. The heart was fairly steady, at a rate of about 60. Dr. J. M. Thomas entered the subject's room and asked if he was comfortable. The patient said, "All right, but the belt is a little tight." Moderate acceleration occurred for 4 beats, and then deceleration. Dr. Thomas stepped out to call in Dr. M. R. Kaufman. Both entered the subject's room, at *KT*. As they came in there was an acceleration lasting about one third of a minute, which ceased when Dr. Kaufman loosened the belt. After Dr. Kaufman went out, at *k*, Dr. Thomas sat in a chair, waiting. The heart remained fairly steady for about two minutes, at a rate of about 60, but was less regular than when the patient was alone in the room.

At *G*, Dr. Thomas asked, "How is your golf game now?" The subject answered, "Well, pretty tough." Moderate acceleration occurred and lasted about two thirds of a minute. At *W*, Dr. Thomas asked, "Is your wife working?" The subject

said, "Yes. It's hard for her with me here." Tears came to his eyes, and he spoke more about her for a half-minute. He looked anxious, and his voice sounded tearful. There was slight acceleration for only 4 or 5 beats; then the rate again became about 60 and remained steady for over a minute. There was much less acceleration than to talk about golf, and the heart was steadier while expressing regret about his wife's having to work than during any other conversational period. Dr. Thomas waited about a minute for the subject to recover from the expected acceleration, which had not actually occurred, and then, at *H*, asked: "Did you mind coming over here?" (meaning to the laboratory for the test). Subject: "Yes, a little. I felt somewhat apprehensive." Dr. Thomas: "About what?" Subject: "Oh, just generally apprehensive." There was moderate acceleration, somewhat similar to that accompanying talk about golf. At *t*, Dr. Thomas left the room. The heart soon resumed the steadiness of rate characteristic of this patient when left alone.

#### UNSTEADINESS OF THE HEART AS REPRESENTED BY THE PERCENTAGE CHANGE PER BEAT

For the comparison of one portion of a heart record with another with respect to unsteadiness, a number of conventional measures of dispersion could be suggested, such as the average deviation from the mean, the standard deviation and the coefficient of variability. For certain purposes these are convenient statistical devices. Fleisch and Beckmann<sup>2</sup> have published a paper in which they considered the standard deviation in records similar to ours from the standpoint of the cardiologist. We have surveyed some of our material with these particular statistical tools, but not exhaustively; that is, the data have not been exhausted. When one considers that two overnight experiments or ten two-hour experiments provide records of about 100,000 beats, on which one can measure the duration of each heart cycle, it is easy to see that one might become bogged in an interminable series of statistical calculations.

In this report we are concerned principally with the unsteadiness of the heart rate, and for this purpose we have calculated the actual change in the duration of a heart cycle from one beat to the next rather than the deviations from a mean.

There are portions of records, for instance, during which the heart accelerated in about half a minute from a duration of 1.2 seconds per cycle to a duration of 0.67 second per cycle, which means, in the ordinary mode of expression, from 50 to 90 beats per minute. Yet the acceleration may occur in a smooth and steady curve. The average change per beat and the average deviation from the mean would be quite different figures; we use the change from beat to beat to measure the unsteadiness.

2. Fleisch, A., and Beckmann, R.: Die raschen Schwankungen der Pulsfrequenz registriert mit dem Pulszeitschreiber, Ztschr. f. d. ges. exper. Med. **80**:487, 1932.

The average of these successive beat to beat changes can be expressed as a percentage of the average duration of a heart cycle during the period covered. The figure so obtained is what we call the "percentage change per beat." For example, fifty successive heart cycles might have an average duration of 1 second, exactly. The first cycle might last 1.05 seconds; the next, 1.02 seconds; the next, 0.92 second; the next, 1.03 seconds, etc., giving the series of differences: 0.03 second, 0.1 second, 0.11 second, etc. If the average of these forty-nine differences were 0.06 second, the change per beat for that fifty beat period would be 0.06 second, and the percentage change per beat, 6. If the same average difference (i. e., 0.06 second) was observed in another period during which the average duration was only 0.5 second, the "percentage change per beat" would be 12.

COMPARISON OF PSYCHOTIC, NEUROTIC AND NORMAL SUBJECTS  
WITH RESPECT TO UNSTEADINESS OF HEART RATE

For this report we have used the figure for percentage change per beat as a measure of the unsteadiness in heart rate, for the purpose of comparing the behavior of the heart in different types of subjects during personal interviews. Before proceeding with this comparison, we shall review the simple facts which can be seen by crude inspection of the graphic records. The general appearance of the heart record has already been discussed, and attention has been drawn to the relative steadiness of rate in psychotic patients as compared with that in normal subjects. We have subsequently had an opportunity to include in our comparisons records obtained on neurotic subjects in the service of Dr. Stanley Cobb, at the Massachusetts General Hospital, and we can say that the neurotic subject shows much more responsiveness in fluctuations of heart rate as one talks with him about his troubles than does the psychotic patient. The neurotic person, indeed, may show even more responsiveness than the normal subject, but this is roughly in accordance with his more emotional behavior. It will be recalled that psychotic patients were found to give an almost opposite result; that is, the heart rate tended to be relatively steady and slow during the exhibition of so-called emotional behavior.

It seemed worth while to examine with some care the finer details of these records, particularly with respect to the unsteadiness, and it was for this purpose that we used the calculation of the percentage change per beat.

We compared the records of fifteen psychotic patients, twenty neurotic patients and fifteen so-called normal persons, mostly physicians and nurses. The cardio-chronographic records were made during personal interviews between the subject and the physician. The interviews were not standardized, but they agreed in

general, in that they were directed at the discovery and discussion of emotional problems. They lasted an hour or two.

For the calculation of the percentage change per beat five separate portions (each 50 beats in length) were selected on each record, the aim being to select by inspection the most diverse sections of the record—one piece, slow and steady; another, rapid and steady; one, slow and irregular; another, rapid and irregular, and a fifth section of what seemed most characteristic for the subject. The duration of each of these two hundred and fifty heart cycles was measured, and the percentage change per beat was calculated separately for each of the five portions and then combined into an average for the person. The figures are displayed for graphic comparison in chart 2.

The most striking feature shown by chart 2 is the accumulation of psychotic subjects at the lower end of the scale and of neurotic sub-

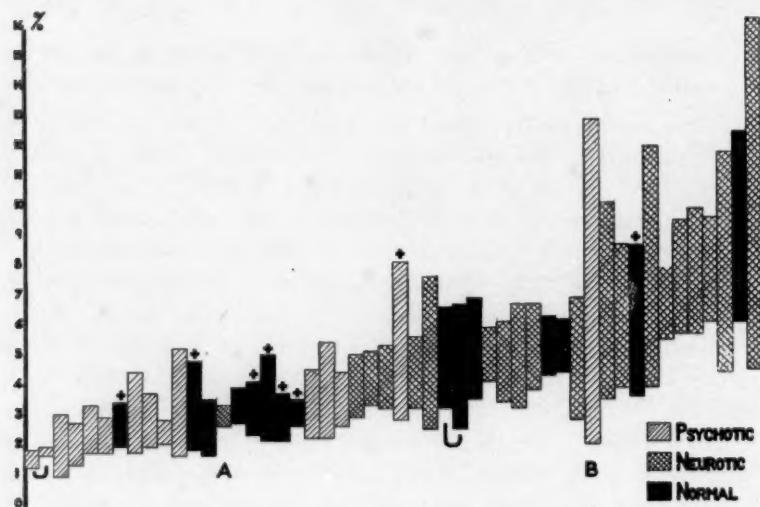


Chart 2.—Percentage change per beat. Each column represents the range of unsteadiness of the heart rate for a particular subject in five samples of a record made during a personal interview. The ordinates represent the percentage change per beat.

jects at the higher end. The psychotic tendency is toward steadiness of heart rate; the neurotic, toward unsteadiness.

The percentage change per beat for patients of the psychotic group averages 2.9; for those of the neurotic group, 6, just twice as great, and for subjects of the normal group, who are scattered rather widely on the chart, 4.4.

It should be borne in mind that most of the psychotic patients whose records are summarized in this chart were classified in the affective group and that they exhibited during the experiments the sort of behavior which leads to that diagnosis. Even the schizophrenic patients

showed overt emotional behavior; yet the heart rates ran, on the average, remarkably steady.

Two striking exceptions are shown on chart 2. The heart rate at *A*, which is exceptionally steady for a neurotic person, was observed in a married woman with phobias about her husband's safety. Although she was not considered psychotic at the time of this experiment, it is perhaps of some significance that she had been in a state institution two years earlier, with an affective psychosis.

The other striking exception, at *B*, is worthy of detailed report. The man was in a typical state of agitated depression—rubbing his hands, shuffling his feet and speaking in a mournful tone and distressed accents. While he maintained that behavior, his heart was not unsteady, as shown at *B*, but stayed steady, as in the other psychotic patients. In this particular experiment he had been taking a Rorschach test. He had responded in the typical depressive fashion, with pedantic attention to detail and denial of whole responses, maintaining meanwhile his affective display, while his heart beat steadily with about 3 per cent change per beat.

He started a discussion with Dr. Beck, who was giving the test. He ceased his hand-wringing, agitated behavior and spoke in a mildly animated conversational tone, as in a normal argument. It was then, while he had temporarily stopped the psychotic affective display, that the heart showed the high percentage change per beat indicated by the top of column *B* in the chart.

Besides these exceptional cases a few other interesting items may be pointed out by means of the chart. It may be of special interest to the medical profession to note that most of the physicians, who constituted half of our normal subjects, are placed by this chart among the psychotic subjects. They may be located on the chart by the crosses. The steadiness of heart rate in physicians during personal interviews perhaps may represent a professionalized attitude.

We had two pairs of twins among our subjects. To judge from physical resemblances, both pairs were probably monozygotic, although we do not have the conclusive evidence from the obstetricians. The pairs are indicated by the symbol *U*, and the figures representing percentage change per beat are so nearly alike for each member of a pair that they fall into contiguous positions on the chart.

#### GRAPHS FOR WAVE DISTRIBUTION

For the more effective comprehension of the individual heart records, we tried to devise a means of expressing in a single figure for each person a kind of abstract representation of how his or her heart usually varies during an interview. The data already given on the percentage change per beat are the result of such efforts. However, some more graphic representation is also needed of how the different sizes of waves are distributed in a heart record. Nothing can quite take the place of the complete record itself, but something is needed to epitomize the full record. For this purpose, we use wave distribution graphs. Such graphs are shown in chart 3.

The graphs are constructed in the following fashion: From the measurements of the representative two hundred and fifty cycles for each subject, one records each change of direction (acceleration or deceleration) amounting to 0.01 second or more and sorts them by magnitudes. The classes were as follows: 0.01 second, from 0.02 to 0.05 second, from 0.05 to 0.1 second, from 0.11 to 0.2 second, from 0.21 to 0.3 second, from 0.31 to 0.4 second, and 0.4 second or more.

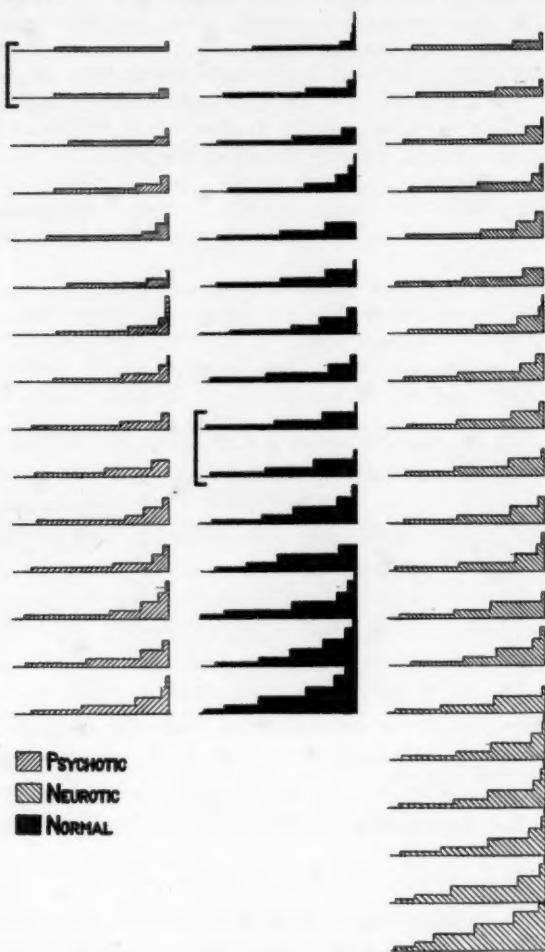


Chart 3.—Graphs of wave distribution. The ordinates represent the magnitudes of "change of direction," and the abscissas, the distribution of these magnitudes per hundred "changes of direction."

A frequency chart is then constructed on a scale of 100 per cent, whereon one indicates by appropriate heights from the base line the proportions of the different magnitudes of changes of direction. To illustrate by the extremes shown in chart 3: M. S. (top graph, left column), of each hundred changes of direction had twenty-seven of only 0.01 second, seventy-one of the next magnitude (from

0.02 to 0.05), two of the third magnitude (from 0.06 to 0.1) and none greater than that, while L. (bottom graph, right column), of each hundred changes of direction had three of the least magnitude, thirteen of the second (from 0.02 to 0.05) and twelve of the third (from 0.06 to 0.1), while the other three-fourths were far beyond the range of those of M. S.—namely, twenty-six, twenty-five, fifteen and six, in the successively larger magnitudes. These are not values per beat but values per change of direction. On the average there is a change of direction in some degree for every two or three beats.<sup>3</sup>

A series of these wave distribution graphs, one for each of our fifty subjects, is given in chart 3. They may serve to epitomize in a more comprehensible fashion certain salient characteristics of the heart records of these persons and to give a clearer idea of the differences between psychotic, normal and neurotic persons. It is of interest also

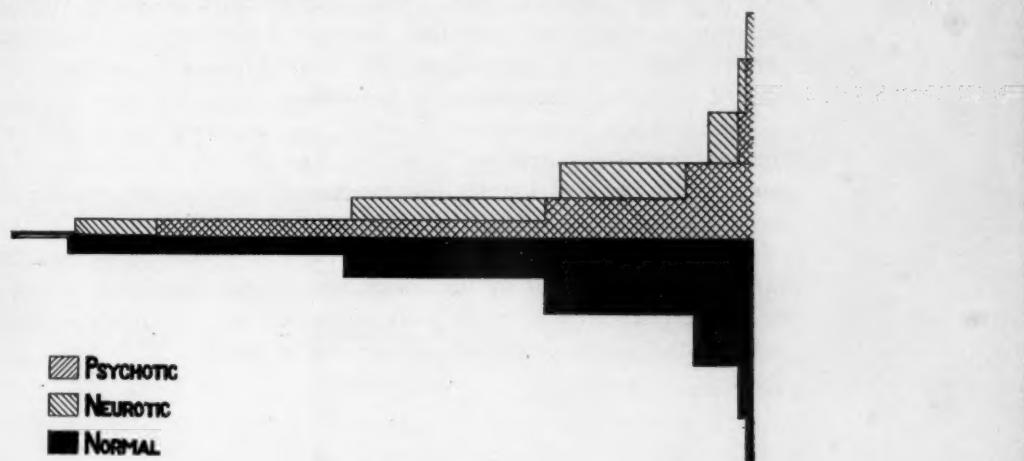


Chart 4.—Wave distribution graphs showing group averages. The members of each group are combined in a single graph, constructed as in chart 3. The graph for the normal group is inverted here for convenience in comparing it with the graphs for the other two groups.

to observe the like records of the twins, which are indicated by brackets on the chart.

In chart 4 the three groups of subjects are combined for comparison of groups.

Study of the waves on the heart records and their representation in this fashion emphasize again the tendency of the psychotic person's

3. When attention is given in this meticulous way to every minute acceleration or deceleration, one picks up the respiratory rhythm—two changes of direction, or one wave about every fifth beat—which in most subjects is obscured on simple inspection by the relatively larger waves, from other causes. This respiratory rhythm can be accentuated by slow, deep breathing.

heart to remain steady or to accelerate and decelerate in relatively shallow waves, as compared with the tendency in normal and in neurotic persons. There is, however, no difference demonstrable in these graphs between normal and neurotic persons, in contrast with the difference shown in chart 2 with respect to percentage change per beat. That is, the waves are about alike in amplitude in neurotic and normal persons. Neurotic subjects do show narrower waves in general, and therefore more per minute—which fact is not represented in charts 3 and 4 but is reflected in the percentage change per beat, shown in chart 2.

#### SUMMARY AND CONCLUSION

The principal conclusion to be drawn from these observations is that psychotic patients, even when reacting with so-called affective behavior in a personal interview, maintain a steadiness of heart rate greater than that of normal subjects, whereas neurotic patients tend toward a greater unsteadiness of heart rate.

The average unsteadiness of heart rate as measured by the percentage change per beat is 2.9 per cent for the psychotic patients in our series, 6 per cent for the neurotic patients and 4.4 per cent for the normal subjects. The different groups overlap each other.

Another point of distinction which rates psychotic persons as less variable is brought out by the comparison of the amplitude of waves on the heart records. On the basis of this comparison of wave amplitudes normal and neurotic persons are nearly alike.

## AGGRESSION AND ANXIETY IN THE DETERMINATION AND NATURE OF MANIC ATTACKS

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### THE MANIC ATTACK AS A REACTION

The psychiatric literature on mania, considered from a clinico-dynamic point of view, has had little new to offer since the time of Kraepelin. It is as if his formulations represented the final word. The main ideas, so well expressed in Kretschmer's work,<sup>1</sup> rest on simple observations and give ready explanations to the manic-depressive phenomena. They concern heredity and constitution and the cyclothymic temperament. This temperament has an inherent tendency to alternate between elation with expansiveness and depression with slowing down. Such alternations may, either for physiologic reasons or because of situational factors, become so pronounced that they incapacitate the patient socially for a certain length of time, which is also assumed to be more or less predetermined.

While in the case of depression transitions between the "psycho-neurotic" depressive and the manic-depressive syndrome have always been recognized, the manic attack has been regarded as being more definitely endogenous or constitutional. This attitude was well expressed by Diethelm, who stated that "dynamic psychiatry has shown that there are always more or less strong dynamic factors" at work in depression, while he put the stress on the endogenous aspect of the manic attack in saying that here the "constitutional factors are etiologically most important."<sup>2</sup> Further on, however, in accord with the teaching of Adolf Meyer, he drew attention to the importance of analysis of the personality in the treatment of the patient for the purpose of alleviating interpersonal and intrapersonal strains.

Psychoanalytic efforts have met with little consideration outside this immediate circle. Strecker and Ebaugh<sup>3</sup> gave a generous account of

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From the McLean Hospital.

1. Kretschmer, Ernst: *A Textbook of Medical Psychology*, New York, Oxford University Press, 1934.

2. Diethelm, O.: *Treatment in Psychiatry*, New York, The Macmillan Company, 1936, pp. 127-135.

3. Strecker, E. A., and Ebaugh, F. G.: *Practical Clinical Psychiatry for Students and Practitioners*, ed. 4, Philadelphia, P. Blakiston's Son & Co., 1935.

certain psychoanalytic hypotheses, but I cannot see that these have in any way influenced the presentation of their case material. The reasons for this lack of integration are evident. The analytic theories concerning the manic-depressive psychosis seem particularly involved, and the deductions are difficult to follow.<sup>4</sup>

It is a question, however, whether psychoanalytic studies, in spite of possible sacrifices to "metapsychologic" theory, have not recorded observations of substantial importance to further clinical understanding of the manic attack. Abraham's contribution,<sup>5</sup> which was the first psychoanalytic effort and which constitutes the basis for subsequent studies, was a radical departure from the common textbook statement of the problem. He found in his work with manic patients that the attacks are precipitated by situational factors and that they are to be explained largely by traumatic experiences of the past. The fact that he succeeded, as he believed, in aiding his patients beyond the ordinary "spontaneous" recovery indicated to him the correctness of his assumptions. Thus, Abraham frankly stated that he regarded the manic attack from the same point of view as he would any other "psychogenic" reaction.

The psychoanalytic theories stress the intentionality presumably implied in the manic attack. The patient is "endeavoring" to cope with his difficulties by an attempt at "overcoming the superego." Even so, the attack is usually regarded as a release phenomenon. The patients are happy and self-satisfied, giving free expression to their immediate impulses, as if their "regression" had really helped them to achieve their aims. Like Kraepelin and Bleuler, analysts regard the aggressiveness and irascibility that may be observed as incidental to the expansive and self-confident state of mind of the patients.

Some authors have maintained that there is not a discrepancy between the underlying striving and the manic mood but that the striving is actually reflected in the mood. Schilder, in spite of his kraepelinian leanings with regard to the general nature of mania, dealt with this aspect as follows:

In all manics I have repeatedly found that the elation, the sense of well-being, is repeatedly disturbed by prickings of recollections of painful experiences of the past.<sup>6</sup>

4. Fenichel, O.: Outline of Clinical Psychoanalysis, *Psychoanalyt. Quart.* **3**:42 (Jan.) ; 223 (April) 1934.

5. Abraham, K.: Ansätze zur psycho-analytischen Erforschung und Behandlung des manisch-depressiven Irreseins und verwandter Zustände, *Zentralbl. f. Psychoanal.* **2**:302, 1911-1912.

6. Schilder, Paul: Introduction to a Psychoanalytic Psychiatry, translated by B. Glueck, Nervous and Mental Disease Monograph 50, Washington, D. C., Nervous and Mental Disease Publishing Company, 1928, p. 139.

He said further that "the manic attack is the constant overcoming of this unpleasant past" and that "the stimulus of the painful must be there." He sought to explain the psychologic phenomenology in the following way:

In every thought phenomenon opposing motives have to be overcome. Motive and its opponent must become combined into a unitary attitude. With the decision, or thought conclusion, there sets in release and a sense of well-being. Probably there is associated with this phenomenon a threat to and a liberation of the personality.<sup>6</sup>

Deutsch,<sup>7</sup> though less explicit with regard to the clinical manifestations, gave expression to similar ideas. Her observations of cases led her to conclude that behind the façade of "triumph" there is a feeling of depression of the nature of "something threatens you," which is "drowned out," so to speak, by the mania.

My work has centered primarily on the psychogenetic relationship of the manic attack to the situational circumstances with which the patient had to cope at the time of the onset. The relatively narrow scope of my study and the fact that no attempt has been made at psychoanalytic formulations prevent exhaustive comparison with psychoanalytic findings. My findings, however, tend to confirm the general conclusion that the manic attack represents a reaction to a conflict situation. These can best be set forth in the discussion of the histories in a few cases. An attempt has also been made to approach the problem of what psychologic constellation may determine whether an attack will become a manic attack or a depression.

First, however, it is necessary to discuss what is meant by a reaction to a conflict situation, that is, a "psychogenic" reaction. The accepted test of psychogenic reaction is the time coincidence of external situational changes and the manifest behavior. This concept, however, secures its full meaning only by being contrasted with the concept of endogenous reaction, which is thought to occur independently of psychologic influences and to be due to internal, physiologic changes. By so contrasting the two concepts it becomes evident that the definition of a psychogenic reaction is an oversimplification. Only one aspect is taken into consideration, namely, the relationship between the person and the environment, while the question of constitutional predisposition is disregarded. This expediency is permissible in certain types of study, but when it comes to an inclusive differentiation between persons, the formulation would be insufficient without the postulation of constitutional predisposition. Thus, the outgoing or the shut-in personality, the volatile or the slowly reacting temperament and the intensive or the

7. Deutsch, H.: Zur Psychologie der manisch-depressiven Zustände, insbesondere der chronischen Hypomanie, Internat. Ztschr. f. Psychoanal. 19:358, 1933.

apathetic person may be studied from the point of view of their ways of dealing with social influences and, furthermore, from the standpoint of what social influences may have served to mold the individual reaction tendencies. There is still the question of how the participation of the constitutional factors in the determination of these reaction tendencies can be formulated.

Birnbaum's discussion of this problem<sup>8</sup> gives indication of the difficulties with which one is confronted. His attention was focused on different types of hysteria, that is, the so-called traumatic and the degenerative hysteria. Traumatic hysteria he regarded as having a "psychogenic" etiology, its cause being mainly psychologic factors. In the case of degenerative hysteria the constitutional aspect should be emphasized. However, even in traumatic hysteria one would have to postulate "help causes," that is, a constitutional predisposition.

Birnbaum's formulation concerning hysteria is generally accepted as applicable, on the one side, to normal motivation of behavior with predominance of psychogenic factors and, on the other, to functional psychosis with predominance of endogenous, constitutional factors. Yet it is a question whether this formulation may not be misleading. Neither type of hysterical reaction can be thought of except as a manifestation of the relationship of the individual person to his environment. The one type of patient, however, differs from the other in being generally more "adequate" in his responses, when these are compared with "normal" behavior. While the one type, therefore, cannot be said to be more reactive and psychogenic than the other, it must be assumed that the constitutional predisposition is different in that it favors a more adequate adjustment in the first type than in the second. Similarly, it can be said of the syntonic moods that may be observed in normal persons of an obsessive-ruminative personality make-up that they do not indicate a greater dependence on constitutional factors and a lesser on environmental factors than do the more varied and shifting moods. Persons of the first type, however, assimilate and dispose of environmental changes differently from those of the second. This may lead to different degrees of success, according to the effectiveness of the particular reactions under particular environmental circumstances, but it is impossible to evaluate the differences of such persons in terms of the degree of participation of the predisposing constitutional factors.

From the preceding discussion, it will be seen that when I consider the manic attack as being of "reactive" nature, this does not mean a negation or an underestimation of the significance of constitutional factors. As a matter of fact, these factors must be assumed to be present always,

8. Birnbaum: Klinische Schwierigkeiten in Psychogeniegebiete, Monatschr. f. Psychiat. u. Neurol. 1917, vol. 41, p. 339.

whether or not they have given themselves expression in other members of the family in the form of psychopathologic manifestations.

Conversely, it is implied that a hereditary "taint" per se, or the lack of it, gives no indication as to whether a given psychopathologic condition is an endogenous or a psychogenic reaction. The only way in which this can be determined clinically is by establishing whether the criteria of a reaction as defined for normal and psychoneurotic persons can be found in the psychopathologic manifestations. That is my purpose in this paper on the manic attack. The difficulties frequently encountered in the study of normal and psychoneurotic persons which are broadly implied in such terms as repression of conflict material and resistance to cooperation are met as well in the investigation of the manic attack. The exuberance of the psychopathologic manifestations adds to the difficulties of analysis, but it should not invalidate the signs of reaction that can really be established.

#### REPORT AND CONSIDERATION OF CASES

CASE 1.—An attractive married woman aged 27, in whose case there was no history of familial mental disease, had a brother three years her junior. She had grown up in the setting of a well-to-do home. She was said to have played normally as a child and to have obtained good grades at school. After high school she studied art and then traveled in Europe for a short while. After her return she began to work in a bookstore and continued with this until marriage. She was considered a stable, optimistic person, with many friends of both sexes. She had married three years prior to onset of the psychosis and ostensibly had lived a happy life with her husband. Further study of the case, however, revealed that both her sexual desires and her social aspirations had been frustrated; because of this she had sought extramarital gratifications. After the birth of a baby she passed into a state of depression in which her contempt for her husband and hate for her child became evident. She recovered after five months, without insight into her feelings toward the child and without adjustment to her husband. She then began to show increased activity. She became interested in religion but soon centered her energy into arranging a fashion show, which constantly grew in scope until she had to be returned to the hospital. In spite of the obvious manic condition, she had shown good administrative ability, and it was difficult to say when the plans were definitely out of bounds. She was enthusiastic and professed to be enjoying herself, but she was tense and overtalkative, as if hiding her disappointment, and became upset easily if frustrated. When returned to the hospital, she was haughty and demanding. While heretofore in the manic phase she had said that everything was all right with her husband, she now began to talk about divorce and made attempts to seduce the physician. The good rapport that had been established with her during her depression facilitated a continued study of her case. At the same time, her husband, a naive and unimaginative man, who had been practically ignorant about sexual intercourse, began to show more understanding in this field as well as in others. The patient was soon permitted to take trips home, and a reasonable harmony was finally reached, after six months of illness.

Most of the material that was elicited from the patient during her depression concerned her husband and her relation to him. Her hatred of her child was hinted at only indirectly. The husband gave the information that the patient had been oversolicitous of the child during the first six weeks after birth, fearing lest something terrible should happen to it. The patient said that she had been worried about not being able to take proper care of the child and about how she could preserve her attractiveness. It was only toward the end of the manic phase that she was able to discuss openly her feelings toward the child. She told the physician that on one occasion, just before her admission to the hospital for the first time, she had gone up on the roof of the house with the child in order to jump off but had decided against it at the last moment.

Even though she had expressed herself about her husband with considerable frankness during the depression, it was not thought at the time of her discharge that the relationship between her and the physician had been sufficiently frank to permit more than a limited discussion of the case with her husband. Much more was achieved toward the end of her second stay in the hospital.

The immediate problem, as judged from what could be observed and from the patient's own statements, seems to be clear. The patient was a young, vivacious woman with strong appetites, already restricted by the narrow scope of her marital life and now still more curtailed by the birth of a child. In addition, she had to cope with what she called her "unnatural" hatred of the child. She discussed her marital situation during the depression but emerged from it without having settled her relationship to her husband with him or that to her child with herself, but believing that she could deal successfully with the situation. When viewed from the latter half of her manic attack, with the frank resumption of the problems of her relationship to her husband and child, the first half seems to represent an eager attempt first at a conciliation for her conscience and then at securing satisfaction through social self-assertion. The latter part of the attack was to a certain extent a surrender, in so far as she was again willing to discuss her difficulties and accept help. At the same time, however, she showed manic activities in the ward, in directing the amusements for other patients, and in trying out her seductive powers on the physicians. Her relationship to her husband was much better at the end of the attack than ever before, and it seemed also that her child had found a more adequate place in her life.

As far as the nature of the psychosis, from the beginning of the depression to the end of the manic attack, is concerned, there can be little doubt that it presented the criteria of a reaction.

There were the conflict situation at the onset and the concern about her problem, both during the depression and during the manic attack. Finally, there was a settling of the conflict, with the attainment of a reasonable adjustment, as far as could be judged from the point of view of observers and certainly from that of the patient herself.

While during the depression the patient felt more or less unequal to the task of adjusting herself to her situation, in the manic phase she made an aggressive attempt to cope with it. Can the fact that this attempt went out of bounds be explained merely as a result of the "manic mood" having been unleashed, or did her erratic procedure have its roots not only in the tendency to a manic reaction but in the nature of the conflict? As far as this case is concerned, it can be stated only that the magnitude of the patient's difficulties as she viewed them at the onset of the depression caused her tremendous anxiety and that the problems were carried into the manic phase as well. This consideration, together with the fact that the patient during the manic phase was far from showing genuine happiness but was tense and at times displayed definite anxiety or actual dejection, would indicate that the initial anxiety still remained a factor of dynamic importance. It therefore may be questioned whether the manic behavior was not the resultant of two reaction potentialities, namely, intense anxiety about her situation and an aggressive incentive to overcome the factors that caused her anxiety.

The circumstances under which the onset occurred in the following cases would seem to give further substance to this assumption.

CASE 2.—A man aged 35 had several relatives, both on the paternal and on the maternal side, who had been considered nervous and high strung. One maternal aunt had had a "breakdown" after her mother's death but had recovered. A sister of the patient, a few years younger than he, had been in a sanatorium for seven months with a condition that was diagnosed as neurasthenia. The patient's father, who had been a somewhat ineffectual person, died when the patient was in his teens; since then the family had been held closely together by the domineering mother, who at the time of the patient's illness was 82. The patient was the seventh of nine children, two sisters being younger than he. His three brothers were active and aggressive, in contradistinction to the patient, who was quiet and somewhat reserved. He had been doing creditable laboratory work until eight years prior to the onset of the present illness, when his brothers persuaded him to join them in their business. The partnership had been successful until the last few years, when the older brothers began to lag in fulfilling their promises to him. The patient had married six years before the onset of the present illness. While the wives of his three brothers had more or less readily submitted their personal interests to the general family policies, his wife had been unwilling to do so and had given increasingly strong expression to her resentment of the family's high-handed dealings with her husband. It was apparent, according to information from the wife, that the depression, of about eight months' duration, from which the patient had recovered three months prior to the onset of the present manic attack, had had its root in the family conflict. In the intervening three months the wife renewed her efforts to encourage the patient to assert himself.

The onset of the manic attack was as follows: The patient arranged a meeting with his brothers in which he attempted to put the situation before them. In the course of the conversation he became loud and aggressive, and nothing constructive developed. His excitement continued. He set up an office in a

hotel, in order to start a campaign for the purpose of entering politics. The patient was then brought to the hospital. He was overactive and overtalkative, with a flight of ideas. He said he "felt fine." He was "going to become the next mayor of the city," and he was "going to fight the politician" who had brought him here. He was the "king of the mugwumps." He was at times irritable and angry and at times boastful and self-satisfied; for a time he was occasionally slightly sad and perplexed. He was frequently jocose and hilarious but had to be watched because of threats of violence. When he improved, he said he had been playing a game, and he was amnesic for the threats. He said that his wife and family did not get along with each other and that he must take his wife's part. When he left, after having been in the hospital for two and one-half years, he stated that he wanted to straighten out his affairs and then go away for a while. Six months later he again became depressed and was readmitted to the hospital after a suicidal attempt, which proved fatal. No real effort had been made to reconcile the divergent interests.

In this case one recognizes an initial and futile attempt at solving a question to which the patient at no time had been equal owing to his timidity. He then began to play what he called a "game," namely, that of a conqueror. In spite of jocoseness and hilarity, a show of self-satisfaction and the statement of "feeling fine," the affective tension, with easily aroused hatefulness and lurking treacherousness, indicated the resentment and realization of his difficulty.

Though it was only at the onset and at the end of the attack that the patient made explicit reference to the task which he had set for himself, the content of the psychosis throughout seemed to be implicitly related to his conflict; the trend was obviously in accord with the spirit in which he approached it, namely, that of wanting to assert himself and to subdue opposition.

The anxiety of this patient had permitted his relatives to prevail on him until his wife's persistent urging brought him to the point of facing his brothers. The meeting with them, however, quickly took a course that could be characterized as a step of desperation rather than one of calm assertion. It is in correspondence with this that the patient, at the end of the attack, while he maintained that he had to take sides with his wife, still was not able to take the initiative in making a settlement with his brothers.

CASE 3.—A single woman aged 22, with no history of mental illness in her family, although an older sister was said to be emotionally unstable, was the youngest of nine children, one of whom became a nun. Her father died when she was 1 year old. The children were given a strict Roman Catholic upbringing by the mother. Until the economic depression, five years previous to the present illness, they were fairly well to do. Then, severe curtailments were necessitated, and the family, under the domination of the mother, suffered considerable constraint in efforts to keep up to their racial and social ambitions. The situation was a source of dissatisfaction to several of the children, who hesitatingly had been making vague attempts to emancipate themselves. The patient, whose early

development was said to have been normal but whose friendships had never been intimate, was considered to be able and conscientious. She was a student in college when the manic attack occurred.

The events leading up to the psychosis were as follows: She had fallen in love with one of her teachers, a Protestant, who returned her feelings, but both felt it was impossible for them to marry because of their difference in religion. Then she began to ponder on her attitude toward religion and to "lecture" her friends on the logical proof of the necessity of Catholicism. She maintained that in the end the marriage would take place. A manic condition gradually became evident. Her conduct was orderly until she was brought to the hospital, when abruptly she became worse. She was overactive and overtalkative, made puns and showed a flight of ideas. Her mood was one of hilarity, broken by irritability and anger, particularly when she was frustrated. Her condition rapidly reached a climax, with tearing of clothing, masturbation and smearing. The main topics of her talk concerned sex, marriage, religion, her family and science, all in confusion. She was "going to convert the whole damn college." She was "having a damn fine time." There were frequent examples of sarcasm toward others, coupled with self-irony. After about a month she began to quiet down. In the periods that followed, the trend of her talk and behavior remained the same, but her conduct became more orderly; particularly, the hilarity disappeared except for momentary bursts. Although she still maintained that she "felt fine," her facial expression was one more of concern, even of sadness at times, than of cheerfulness. She became more able to talk coherently about the different topics of which she had spoken, but she could not follow them to a conclusion, though she had tentative suggestions to offer. She seemed to be groping in vain. She said that she felt confused and had a feeling of unreality. She made remarks which seemed to indicate that she did not want to give up her psychotic condition. The patient was discharged as recovered, four months after her admission to the hospital.

As in case 2 one recognizes the outline of a serious social situation at the onset of the psychosis. The patient's background was that of a strictly conventional Roman Catholic home. Through her infatuation with a Protestant of a different race, she, as conventional as her home, had thus suddenly and unpreparedly met a major problem of life in which a compelling urge had come in conflict with an equally compelling obligation to her conventions. Her first attempt at overcoming the difficulties was to try to analyze her own attitude toward religion. As she could not make any change with regard to that problem, her next step, evidently less well oriented, was to try to make other persons accept her religious views. Then followed an interval in which she took the attitude that she had the situation under command. It is of interest to note, however, that the remarks that bore on this mastery implied more a wish than an actuality ("I shall convert the whole damn college"). During this period she was extremely excited, and no definite trend of thought prevailed, although the confusion of ideas remained inside the realm of her prepsychotic concern. As she became quiet, she gave only vague and occasional expression to her "triumph," while her groping became more conspicuous. The different

problems took more definite form. She spontaneously began to discuss them with her physician but was not able to go deeply into any single problem and finally gave it up entirely. The situation with her former friend was, however, no longer acute.

Thus, the sequence of events of this attack follows the outline of a reaction. The problem that gave immediate occasion to the illness, namely, the love affair, subsided automatically with the onset of the illness. The issue that was precipitated with the love affair, namely, the conventional relationship to society, was disposed of not by an actual and constructive solution but by repression.

The motive force of anxiety seems to be well demonstrated in this case, particularly at the beginning and at the end of the attack. At the beginning there was the anxiety implied in the futile attempt to emancipate herself, and after that failure, her desperate gesture at making the world comply with her needs. At the end she withdrew from the whole problem of her concern.

The factor of aggression, which expressed itself first in her attack on the conventional system in herself (analysis of religion), was then turned against the world. The erratic defiance represented, however, also a degree of liberation from conventionality (profane language and smearing), even though she talked more about what she was going to do than what she had done. The fact that she never actually expressed real happiness and satisfaction corresponds well with this. At the end of the attack, aggressiveness again became congealed in her system of rigid conventionality.

Study of the histories in the three cases has revealed that the onset, as well as the course and the conclusion of the attack, was pertinent to the situations of conflict in which the patients found themselves. Schilder, as previously quoted, stated that the painful recollections that are constantly disturbing the manic patient consist of experiences of the past. My own observations correspond with this only in part. It is undoubtedly true that unpleasant experiences of the past stand out significantly during the work with the patients. In my material, however, as represented by the cases discussed, it was the immediate situational problems that dominated the clinical picture.

Furthermore, it seems that the affective forces that determine the manic mood consist of anxiety and, with it, aggression directed toward overcoming the factors causing anxiety. In spite of elation and a show of self-sufficiency, the problem of concern is always with the patient and remains the theme around which the patient's activities revolve until it is solved in one way or another. The erratic and socially intolerable behavior, notwithstanding the reaction, therefore can be said

to be the expression of an adaptive effort. Freud's formula of work being performed in the depression may thus be applied with equal justification in the case of the manic attack.

DETERMINANTS OF THE MANIC OR THE DEPRESSIVE TYPE  
OF REACTION

In the preceding discussion, Abraham's contention that the same "complex" exists in the manic attack as in the depression has essentially been supported. The question then arises why a patient will react at one time with a depression and at another with a manic attack. The common assumption is that such a patient will have a depression or a manic attack according to whether he is on the "down grade" or the "upgrade" in his cyclic alternations of mood when the psychotic attack occurs. The following history exemplifies this in that the manic attack occurred in a person who had always shown a tendency to expansiveness.

CASE 4.—Of a capable business man aged 39 it was reported that "during the depression his business had fallen off tremendously and that he had worried a great deal because of his inability to figure out ways and means of keeping it at its usual standard. Any recent character changes were simply an exaggeration of his usual self in that he had become extremely elated and had conceived ideas of a grandiose nature concerning his ability to end the depression." The patient was not depressed before the onset of the manic attack, although it was noticeable that he was apprehensive about the future.

Although the assumption may contain essentially facts, it does not cover important clinical observations pertaining to the manic-depressive attack. A few instances indicate the type of observations to which I refer. Besides the more dubious observations on the habitually depressed patient who responds with a manic attack to a complicated situation and, vice versa, on the habitually expansive person who responds with a depression, there are cases in which influences other than the purely mechanistic-biologic are unquestionably in evidence.

CASE 5.—With a woman aged 38, whose depression had been stationary for some time, the discussion of a certain topic brought about an immediate change. For the first few days she seemed to improve, but within a week she showed signs of hypomanic excitement. When the probable cause of this was pointed out to her, she instantaneously became depressed again.

CASE 6.—A girl aged 20, who was improving from a severe manic condition, was depressed when she was alone in her room. She became manic when with other patients and the nurses in the hall or when some one came into her room.

The inference from these and similar cases necessitates a modification of one's view of the onset of the manic attack. The reactions that occurred were evidently responses to changes in the psychologic situ-

tions. Furthermore, at the moment when the manic phase appeared in these cases, the constellation of psychologic factors must have been in accord with the constellation to be found in the case in which the manic reaction seemed to be growing out of the expansive personality. Otherwise, one would be compelled to accept the rather forced idea that one is dealing with two essentially different types of manic reaction. It seems then that in certain cases the patient may habitually or in cycles take an attitude which under provocative circumstances serves as a foundation for manic development and which in other persons may be formed in a short time or momentarily as a response to such a situation.

In some of the cases of manic excitement studied the psychologic connections of the train of events at the time of onset were indicated fairly clearly in the objectively observed behavior. The patients themselves, however, did not give any statements that would point to their own experiences of what took place. One such case will be described briefly. The cases of two other patients who were able to give an account of what they conceived to be the circumstances surrounding the onset of their manic reactions will then be reported in more detail.

**CASE 7.**—A woman aged 26 had had a disappointment in a love affair and thereon had become the mistress of another man, whom she married after having become pregnant by him. During pregnancy she showed gradually increasing signs of depression, with hatred of the unborn child and of the husband. She had to be hospitalized soon after delivery. The husband, whose attitude all through the wife's pregnancy had been irresponsible, then secured a minor position in a small town and showed serious intentions of living up to his responsibilities. The patient recovered after about two months and remained well for about one and one-half months, taking care of her house and child. However, she was not content with her husband and the small town life they were living. When she was requested to help market an invention of some promise, she threw herself eagerly into the work, visualizing the return to a more interesting environment and the advantages of economic freedom, which also, as was evidenced later, implied freedom from her obligations. The work proceeded slowly, and the patient became more and more pushing in her attitude, until she was finally in a manic condition.

The psychologic situation in this case seems to have been as follows: At the time when the manic attack began, the patient's situation was tolerable, although it left considerable to be desired. (A comparison with the psychologic situation at the onset of her depression is of interest. The outlook, all in all, was gloomier, particularly after the initial disappointment). The new opportunity that seemed to be in the offing spurred her initiative and put her actual situation in a still poorer light than before. The inertia of the business proposition increased her apprehension with regard to the outcome and drove her beyond her capacity for deliberate progression. Her general attitude, however, remained one of aggressiveness and determination to achieve her triumph, and the manic reaction ensued.

In case 1 one may distinguish the outline of a similar development. Although it was evident to observers that the conflict of this patient was not solved at the end of her depression, she herself was apparently hopeful of being able to handle the situation. It was on the basis of this hope that she began pursuing the plans which took her further and further into her manic attack.

The onsets of the manic attacks in cases 1 and 7 have the following features in common: The circumstances under which the patients were living were unsatisfactory, although not sufficiently so to cause continuation or recurrence of the states of depression they had had. They were eager, therefore, to alter the conditions. The situations in which they found themselves were thus conducive to initiative and action, and as opportunities were given in each case, they proceeded to carry out their plans. With the progress, however, apprehension concerning the outcome developed, and the manic attack, the resultant of aggression and anxiety, ensued.

Study of the next two patients, who gave definite statements with regard to the "causes" of their attacks, gives a firmer basis to the preceding interpretation and a better insight into the "mechanism" of the onset of the manic attack.

CASE 8.—A girl aged 19, because her impoverished family thought she ought to join her social group, was working hard to prepare herself for admission to a club. Another recent venture of a social nature had not been successful. At the last moment she felt (and with good reason) that she would fail. She became desperate and attempted suicide by taking ammonia. She was admitted to the hospital. After about four months she had improved so much from the depression that she could be discharged. The plan, of which she ostensibly had approved, was that she should go west to stay with a friend. After a two day automobile drive with her father, however, she refused to go farther, as she felt that she was going to become a burden to her friend. She did not want to visit her "except as an equal." She returned to the hospital and was still depressed, but somewhat more active. In the course of a few days she became hypomanic but remained cooperative in every respect. She expressed the firm belief that she had a chance of becoming the President of the United States. The mission she had to fulfil was, first, to unite the different races in this country and then help other peoples to understand each other and thus prevent war between them. The patient clung to this idea for some time. Little by little, she gave in to the pressure of dissuasion and finally accepted a plan to take up office work in the city in which her father was living. Her ambitious fantasies gradually became more modest and receded into the background, although she continued to follow the same altruistic trend. She was discharged after two months, and it has since been reported that she has adjusted satisfactorily, showing more appreciation of the limitations of her capacity.

The patient was the youngest of three children, the other two being capable and self-sufficient young men. Her father was an extremely energetic and rather impatient man—amiable and with many friends. In spite of severe financial reverses relatively late in life, he had not lost courage but was actively trying to reestablish himself. He had had two manic attacks but seemed to have

learned by experience, and his approach to life was perhaps sounder and more adequate than before. The patient's mother was a woman of high culture and lofty ideals, who had withdrawn more and more into a narrow circle and gradually had become a heroic-tragic invalid, finding solace in nature and in being admired for her altruistic attitude. A love affair on the part of the husband years ago had caused a partial separation, which became more definite, although not complete, when the financial reverses came. The patient's father took up the struggle to reestablish himself, and the patient and her mother went to live with the maternal grandmother. The thought of divorce had always been horrible to the patient's mother, who rather had been inclined to talk about "holding the family together" without, however, doing anything actively to achieve this aim. It seemed evident that she had done everything to keep her daughter close to her. On several occasions she had broken up the few friendships her daughter had with other women, and she had also put obstacles in the way of her education. However, she praised her daughter for her cleverness and her altruism. The patient's father did not seem to have taken much interest in the daughter, partly because of having been busy helping his sons to emancipate themselves and partly because of the rebuffs from his wife, the patient and his mother-in-law. When, however, the patient became depressed, his initiative was aroused, as he felt that now the time had come for him to be of help to his daughter too. The grandmother had sensed that the patient's education was wrong and had tried to push her into a large circle of acquaintances, not understanding, however, the girl's sensitiveness. She was the person responsible for the task the patient had undertaken in the struggle for which she had failed. Before her psychosis is outlined, a few more pertinent facts should be stated. The patient's appearance was striking. She was well built and attractive; yet her appearance was lacking in charm, as her movements were awkwardly mannish. Several of her mannerisms were clearly copied from her younger brother, of whom she was fond. She had never had any boy friends but had had "crushes" on a few women, most of whom were older than she. She had had considerable success in athletics.

The patient's complaints after her admission to the hospital were that "she was no good," that "she was a failure" and that she had not utilized the chances that had been given her. After rapport had been established, she said that she "had never really grown up" and spontaneously qualified this in different ways, showing considerable insight into her dependence on her mother and her inability to decide for herself. When her mother was discussed, she gave evidence of recognizing how her mother had put obstacles in her progress and gave examples of it spontaneously. She was inclined, however to put the blame for this on her grandmother, who received considerable criticism for her domineering attitude. When one tried to discuss future plans involving emancipation from her mother, she became even more vague and showed a marked tendency to drop the subject and to begin accusing herself of having failed in her attempt to hold the family together. When, under more pressure, exerted primarily by her father, she finally began to formulate definite plans, it was ostensibly with the ultimate goal of uniting the family. She also demonstrated the similarity of her attitude toward responsibility to that of her mother when, toward the end of the depressed phase (at the time of the final formulation of her plans), she presented symptoms of invalidism ("something wrong with her heart"). The patient's relation to her father can be described best perhaps as being characterized by a feeling of "awe." While his life did not seem to be guided by the same idealism as that of her mother, the abundance of his vitality impressed her. In moments of relatively bright mood and in her hypomanic condition, she used her mother's supercilious expression about him—"he is so tremendous."

The setting of the patient's psychosis can thus be characterized briefly: She had had an increasing feeling of getting nowhere, partly because of love of her mother and dependence on her and partly because of her mother's subtle domination, while her brothers, helped by the father, were making themselves gradually more independent. Her labors leading up to the depression were strenuous, though utterly timorous and half-hearted, attempts at joining them. Her often stated wish of seeing the family united and her hopelessness because she did not succeed in effecting it not only were an imitation of her mother but expressed the need of the father's support, for which she did not dare to ask as the situation had been. This could be attained only if the father was first "tamed," so to speak. When the patient left the hospital to go west with her father, it was obvious to both her family and the hospital staff that she was apprehensive; thus her refusal to continue the trip did not come as a surprise. However, to her the refusal represented a desperate effort, and her surprise was great when she saw the effect. It is to this event that the patient referred the onset of the manic attack. Her father, disappointed because of the frustrated plans, was nevertheless pleased by the fact that she had asserted her own desire. He took the opportunity to talk frankly with her, and she responded well to this talk. He felt that the trip had helped him to become better acquainted with his daughter. Thus, it can be said that the patient had discovered that she could exert her will against her father; in other words, she could "tame" him. She asserted her wish on another occasion on the same trip. Her father had wanted to stay overnight with a friend of his. The patient refused to do so, as she did not want, she said, to "sponge" on his friends. As a consequence, they stayed in a hotel. This had always been her mother's attitude toward her husband's friends. Not only did she wish not to "sponge" on them but she maintained (without good reason) that they belonged to a loose set.

One finds, then, that the patient, afraid of taking the trip, succeeded in interrupting it by the help of a face-saving excuse. At the same time, she succeeded not only in superseding her father's intention but even in gaining his admiration. By the second assertion it was as though she had also succeeded in making her father acknowledge her mother's point of view. It would have appeared to her then that the first step toward family unification had been taken.

It may be asked if the assertions were not in themselves signs of an already existing hypomanic condition. This does not seem probable, when one considers that there was no sign of her elation until several days after she returned to the hospital.

The further development of the manic attack followed the pattern outlined in the first part of the paper, in which I have pointed out that the manic reaction can be regarded as the resultant of aggression, on the one side, and of an underlying anxiety about defeat, on the other. In this case, the patient soon perceived unconsciously the difficulties that lay ahead of her as far as the family situation was concerned. Also, her lack of normal socialization was such that she could not at this time envisage every day work of an ordinary type in an unselected group of persons. Becoming the President meant a victory with regard to the family situation, as well as a solution of the unpleasant problems of future work.

CASE 9.—A single woman aged 33 was admitted to the hospital because she had become excited on the preceding day, presumably on account of overwork. The patient was overtalkative, somewhat defiant, yet friendly, and slightly erotic in her behavior. She rapidly became quieter and was able to leave within a month. Her mother could give little information about the onset of the daughter's illness, although it should be noted that at one important point she distorted facts to a certain extent.

Some time after her discharge the patient gave the history of her past life, the immediate pertinent facts of which were as follows: At the age of 21 she had had to terminate a love affair because of her fiancé's infidelity to her. After that she was depressed for about two months. She kept away from men for some time. She had several love affairs afterward, however, but none was as serious, in spite of the fact that she had met many "nice men." She had flirted with them, had been on petting parties and had experienced sexual arousals but had never had sexual intercourse. The patient had always succeeded well at home, though at times the situation was trying. When she was in her teens, relatives had given her financial support, so that she could obtain a college education. This had caused considerable jealousy in the family. Her mother was a domineering person; the patient and her father frequently gave in to her in order to maintain peace in the home. The patient had had several episodes of mild depression prior to her present illness.

About two months previous to the beginning of the patient's present illness, she had met a young man with whom she had gradually become more intimate, although they had not had sexual intercourse. She often stayed awake for several hours at night because of sexual tension. At the same time she had had to carry on rather strenuous work during the day. One Sunday, about two weeks prior to admission to the hospital, her friend had given occasion for jealousy on the patient's part. He had had to take a young woman, the guest of his employer, on a hiking trip, on which the patient also went. His being with the other woman was no surprise to the patient, and yet she became jealous. For some time she and her friend had been talking about parting, as his position was uncertain. Furthermore, she felt that their relationship took too much out of her; in addition, she was afraid that they might not have strength enough to keep inside "the limits." At the time of onset of the illness, they had determined to separate. Two weeks before, on the day following the hiking trip, the patient had a back-ache. On the recommendation of a nurse she called in an osteopath, who gave her a few "treatments." Her mother, who knew of it and whose brother was a physician, said she did not want her daughter to continue and notified the osteopath

of this. (The mother explained to the hospital physician that the osteopath could not come to see the patient because he had injured his back. The fact was that he had injured his back but had been well again on the following day.) The patient referred the onset of the manic excitement to the following episode: She was extremely angered with her mother's interference, which she considered unfair; yet, as usual, she was much afraid of her mother. At a moment when she was on the second floor and her mother on the first, she called to her mother and said that she (the mother) had had no right to do what she had done. The osteopath helped her, and she wanted her mother to tell him to come to see her again. The mother did not answer.

One sees here a reaction contrary to the patient's normal patterns. It seems, however, that it gains explanation from the setting in which it occurred. She was worn and tense from the strain under which she had been. Her amorous (and emancipatory?) episode had been brought to a conclusion, and she was now treating herself successfully for it by having her back rubbed. When the encounter took place, therefore, she had an intense feeling of justification on her part and of unfairness on the part of her mother, and it was apparently this feeling that established the basis for the defiant self-assertion. Her unusual self-assertion caused her customary fear of her mother to increase. The psychologic constellation, which in cases of predisposition may lead to manic excitement, was thus present, namely, a tension between aggression and anxiety. The circumstances under which the reaction took place make the preceding conclusions probable. It is possible that another factor was present. Treatment by the osteopath may have represented a continuation of her love-play with her friend, in a somewhat attenuated form. (She reacted strongly to physical examination at the hospital.) The mother's interference may therefore have represented an accusation of immorality, which thus gave increased impetus both to her self-assertion and to her anxiety.

In comparing cases 8 and 9, one finds similarities and dissimilarities. In both cases the attack referred to an episode of self-assertion. Yet, in case 8 the manic development had its inception only indirectly in the assertion itself, in so far as the effect of the assertion on the father helped to promote the excitement. In case 9 the connection was direct. The onset differed also in that in case 8 the development was gradual and in case 9 explosive. The first, more important, difference may be reduced to the following psychologic formulation: The result of the first patient's assertion was unexpected encouragement of her endeavors and assurance of her worthwhileness by a person representing a world from which she had been excluded. Her father's response restored to her a feeling of security, as it was approval of the righteous and idealistic attitude she had been maintaining before and all through her illness.

In case 9 there also was a situation in which the patient had a certain reason to feel morally secure. She had been carrying on her work in spite of fatigue. She had been victorious in breaking off a relationship which might have been open to criticism. She was taking a form of treatment which was restoring her to health and which had been recommended by a nurse. Thus, there was a basis for her righteous indignation at the demand of the mother.

The difference in development at the onset in the two cases is explained simply by the fact that the situation in the first case would precipitate satisfaction and hopefulness with the implication of planning and of efforts at carrying out the plans. The more concrete form the plans took the more anxiety would be mobilized, thereby causing the pathologic development. The second situation was conducive to an emotional eruption which immediately mobilized the fear that the patient had always had of her mother. Also, the feeling of guilt that the patient may have had in regard to the osteopath may have been stirred up suddenly by her mother's interference, thus reenforcing her acute anxiety.

Of the four cases (1, 7, 8 and 9) that have been discussed, case 9 is perhaps the most striking and telling. In cases 1 and 7 a degree of security had been gained. These patients had attained a basis from which to proceed in order to allay their inner unrest and reach a more satisfactory adjustment. In case 8 a similar development had been under way when the conquest of the father changed the patient's outlook in a moment and gave her, too, a foundation for hope of further achievements.

In case 9 the manic phase was particularly dramatic in its development. The usual reaction of this patient to difficulties had been in the nature of depression. Hopelessness and exasperation could have been expected. A nuance in the constellation of factors, however, precipitated a reaction of aggressiveness and censuring of others, instead of self-censuring and relinquishing of effort.

The last two cases have an important factor in common. In both the onset was referred to experiences which in themselves are well known psychologic reactions with adequate psychologic connections, with regard both to antecedence and to subsequent developments (quite apart from the aspect of what is specifically psychotic). In case 8 there were discouragement because of failure, the pleasant surprise of approval and achievement and the ensuing hopefulness and initiative. In case 9 there were the tense struggle for maintaining self-mastery and equilibrium, the thoughtless interference (and subtle accusations?) on the part of the mother and the righteous indignation and defiance of the patient. The patients' own appraisals of the causal connections are

in entire correspondence with the interpretative explanations of the developments, as derived from the study of the past histories and the psychotic phenomena. That holds particularly in the first case, in which much more material was available than in the second.

#### CONCLUSION

In the first part of the paper I have attempted to show that the manic attack represents a reaction to a complicated situation. The study indicates that anxiety, together with a drive to overcome the disturbing factors, constitutes the motivating force throughout the course of the attacks.

In the second part of the paper it was pointed out that clinical experience indicates that whether the psychotic episode is to become a depression or a manic reaction is not necessarily to be deduced from whether the patient is on the "down grade" or the "upgrade" of his cyclic alternations when the traumatic circumstances occur. Situational factors seem to be of importance in determining the attitude which the patient takes to the traumatic experiences and are consequently also of importance in determining the nature of the attack, whether manic or depressive.

Study of the case material leads to the following conclusions: If the traumatic situation implies also the possibility of hope of overcoming the obstacles or the adverse forces, initiative may be aroused, accompanied, however, by apprehension about the outcome. The hopefulness is apparently based on a certain feeling of security. Two cases lent themselves to closer study. In one of these the feeling of security could be traced to restored self-confidence, inspired by the father's attitude. In the other case, the security was in the nature of a feeling of righteousness, justified by the patient's own "proper" actions.

These findings are in accord with clinical experience with patients whose manic attacks occur on the basis of an habitually expansive mood and in those whose attacks occur in the expansive phase of their cyclic swings. The observations also explain how a manic attack may occur paradoxically in relation to the preceding mood.

## Case Reports

### THE MOOD—CONTENT PROBLEM AND THYMONOIC REACTIONS

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A scheme of general psychopathology which may be applied in the study of any item of psychiatric interest has been suggested by Meyer,<sup>1</sup> as follows:

1. *What mental factors and imbalance may do along lines of—*
  - (a) Minor interferences or complaints (wrongly called "neuroses") such as special preoccupations, substitutions and dissociations with attention to the behavior and rôle of special experiences and their hangover or anticipations.
  - (b) Dominating affects and their fixation (pure or impure) with incidental modification of content.
  - (c) Leading topical content disorders from projection, disowning tendencies, compensation, systematization and false crystallizations and fixations.
  - (d) Specific disorders of grasp, panic and puzzle states.
  - (e) Developmental deficiencies.
2. *What poisons and metabolism and special organs and their malfunction can do to the brain and its functions and thereby to the personality.*
3. *What leading structural disorders of the brain can do to the personality.*

This scheme offers a simple, natural and direct orientation in the consideration of a psychiatric problem. It accords well with the general grouping of clinical facts and offers a sound basis for the more specific diagnostic considerations, which should be of later interest in the case.

It is noted from this scheme that a certain tentative contrast is given to affect and content disorders (1 b and 1 c), a contrast more apparent than real since these distinctions are meant to designate main trends only and are in no wise mutually exclusive. Essentially contentless affect states and affectless content disorders are sufficiently rare to excite special comment. They should be considered in the nature of rather pure cultures of conditions usually found in a certain admixture. For example, in depressions characterized by the "pure" diffuse affect of sadness, "blueness" and melancholy there is a prevailing type of content dealing with self-depreciation, unworthiness, sin, loss and poverty, clearly dependent on and in keeping with the dominant mood. Likewise, in states of fixation of content, as in schizophrenic or paranoid conditions, there are commonly present irritability, moroseness, worry and hate, i. e., "impure" affects, or affects with projection, dependent on the content. In both these examples is seen a leading trend in affect or in content, with a dependent or incidental trend involving content or affect, respectively.

1. Meyer, Adolf: Unpublished material used in the introductory course in psychopathology in the Johns Hopkins University, 1933-1934.

There remains, however, a borderline group of cases showing strong affect and content in which the relationship is much more close. In these cases the affective reaction—usually depression, less often elation—is very strong and is best, if not only, elicited in connection with certain topics on which the patient harps continually and which had exerted a decisive rôle in precipitating the illness through their deep anchoring in the organization of the personality.

It is not possible in such cases to speak of affect or content as leading and dominant, and of the other as dependent and incidental. Both are leading and dominant. Each feeds on the other, and each draws its final importance from deep constitutional factors of personality.

As will be shown, such reactions are highly individual, and restoration to health comes, if at all, through (1) the final emergence of the affect factor as more important, or (2) through the segregation of content, or (3) its dissolution through a socialization of the personality.

#### CLINICAL EXAMPLES

Such cases are not at all infrequent. The following examples from the Henry Phipps Psychiatric Clinic of the Johns Hopkins Hospital illustrate rather strikingly such closely knit strong content and affect reactions, their origins in special life problems and personality setting, and the various possibilities as to the outcome.

*CASE 1.—Immediately after the birth of a child a woman became depressed and resentful toward the baby. She attempted suicide with gas. Four years after the onset she has become less accessible and more careless and disinterested, with mutism and hiding the face. A maternal uncle and a maternal cousin committed suicide.*

*History.*—The patient, a Jewess aged 28, who was admitted to the hospital on June 14, 1932, had become ill soon after the uneventful birth of her first child in October 1931. She became irritable, nauseated, unable to eat, could not sleep, cried and did not like to nurse the baby. The husband stated that she did not care for the baby, that she continually wished she had never had it, talked of suicide, and thought she would be all right if the baby would die. The patient said, "It's just having had that baby—if the baby'd pass out, I'd be well right off." Her head felt as though the "world was setting on top of it." One month after delivery a sister-in-law took the baby because it "got on the patient's nerves"; every time the latter thought of the child she felt "horribly depressed," and when she did not think about it she felt "so well every way." The "terrible thoughts" ran on how awful it was to have a baby that got her into such a condition and kept her from sleeping. In contrast she liked to dwell in thought on the good times she used to have with her husband. A month in a hospital did not change the feeling toward the baby, although she felt better otherwise. A trial at home was not successful, and in January 1932 she went to another hospital, where she remained for three months. She ran away from this place to her home, where she was found by her husband attempting to commit suicide with gas. She made another attempt to care for the child, but her feeling against it deepened. She said, "It's like a machine in the back of my head repeating over and over 'Why did I ever have to have a child?'"

*Examination.*—On admission she was well dressed and fairly tidy in appearance; she seemed resentful and at first talked unwillingly. She described her spirits as

being "low" and was constantly preoccupied with the thought of having had a baby and her hatred for it. Orientation and memory were good; she retained only five digits and was only fair at calculation; her judgment and insight were poor. In the hospital she appeared restless, irritable, lacking in interest, brooding, sad and tearful; she refused to speak and remained motionless.

Physical examination gave essentially negative results. The only unusual laboratory finding was a white blood cell count of 10,600.

A recent report from the hospital where she is now indicates that the patient is slow in all activity, uninterested and careless about her clothes; she sits or lies in one position for long periods of time; she answers questions in monosyllables or by shaking her head. She is oriented and denies that she has hallucinations. She makes statements indicating that she is in a depressive mood, entertains suicidal ideas and is sometimes tearful. She often stands with her face covered or with her face to the wall, has to be coaxed to eat, although she seems to have gained weight, and sleeps very well. She is tidy in habits but never helps with the ward work or does occupational therapy. The outlook is regarded as very poor.

*Analysis of Data.*—The patient was the fourth child in a family of five children; birth and early development were not unusual. She stopped school at 16, when she was in the second year of high school, and took a business course. She worked a short time in a bank and then helped in her father's bakery. There were no serious illnesses.

Sex never presented a great problem. She was not disturbed by the onset of the menses and had no dysmenorrhea. At 17 she became engaged and married at 19; she was unusually happy, "never passionate," and was often called "frigidaire;" she took sex relations as a matter of course and occasionally had an orgasm. She never wanted children, and condoms were used without any conflict, but when her parents insisted on progeny she agreed. She became pregnant four years ago and had a miscarriage at six months; her reaction was not marked—"I wasn't sorry and I wasn't glad."

Following a slight automobile accident two months after the miscarriage she became much upset, had a "nervous breakdown," suffered from sensations as of things crawling under the skin, gastric distress, headaches, insomnia and fear of disease, especially cancer. She recovered from this illness in about three months and did not require hospitalization. The second, successful pregnancy came in January 1931.

Her interests were limited and her habits not remarkable. She was usually even-tempered, cheerful and never worried; she "liked to be on the go," and was indulged and humored by her family and husband; she was rather passive, fairly friendly although she had few close friends, quiet and reserved. Without any strong drives or ambitions, she was ineffective, carefree and avoided responsibilities.

The family history reveals a depression and suicide in a maternal uncle and the suicide of a maternal cousin.

Reactions of this type may show photographic recurrence after apparent symptomatic recovery. This is to be expected when, as often happens, the content remains unchanged except in a more latent form after the "recovery." The course of the recurrent illness may not be as happy as the first one. The following cases illustrate the strong fixation of the content leading to chronic "rut" formation or habit deterioration of a serious character.

CASE 2.<sup>2</sup>—*A young man attempted sex intercourse with a pig, after which he was subject to a persistent undercurrent of feelings of guilt. Five years later there occurred a flare-up of intense self-depreciation and preoccupation, with suicidal ideas, blocking of the stream of talk, paranoid delusional ideas involving a body change through a psycholeptic attack, and forced associations based on the content. With ventilation of the material and study of the personality he improved after one year. He returned to work with reduced efficiency. Two years later, there was a recurrence of depression, with loss of his job, with marked paranoid elaboration and fixation of content, mutism, feeding by tube and incontinence, which has persisted for two years with little change.*

*History.*—The patient, a man aged 25, became depressed, dissatisfied with work, apprehensive and felt that people were looking at him. He was slow, work was difficult and he felt that all was lost. After six months he experienced a severe psycholeptic attack, after which he was confused for a short period, then preoccupied, quiet, depersonalized and entertained ideas of killing his father for unfaithfulness to the wife; finally he fled to the mountains, where he was found starved and with a foot badly frozen. At that time he heard the voices of his old companions whenever he chanced to think of them. When rescued and brought to the hospital (April 25 to Aug. 30, 1930) he showed depression, preoccupation with the physical changes which he felt were produced in him by the psycholeptic attack and with sin, marked retardation, blocking of the stream of talk by pre-occupations and forced associations, as looking at a woman or thinking of women always causing the thought, "pig's vagina," to flash through his mind. Improvement set in after ventilation of the content concerning an actual attempt at intercourse with a pig five years before, and the use of the material distributively in an analysis of the personality, the outstanding feature of which was the poor socialization of the sexual-religious development and emancipation from his mother. He returned to work with a subjective sense of well-being, but, according to his employer, with diminished efficiency. He suffered a mild transient panic reaction in September 1931, when he attempted to force the father of his sweetheart to acquiesce in their relationship. This attempt, undertaken to carry out rather literally our general advice to settle his problems rather than to let them remain as constant topics of preoccupation, had carried him almost to blackmail before he sensed the peril of his position.

In June 1932 he lost his job because of economic conditions and was unable to find another; he became depressed and had to be committed to a state hospital in February 1933. In the hospital he appeared depressed, saying, "I can't be happy—just going from day to day—things are bad." He had made two suicidal attempts and begged to be allowed to starve to death. In addition there were strong evidences of a return of the previous preoccupations and elaboration of new content material in his insistence on "physical changes in the head," "thoughts put there" (the head); an evil spirit was put into him, and it said, "Don't eat," "no immortality," "you'll never forget *this* day," and "I'll make an s.b. out of you." When he looked at other patients, they blew their noses; if he thought of his family after he had eaten, harm would come to them; specifically, the sisters would "turn out bad." He went through a period of decreased rapport, had to be fed by tube for four months and was mute. At present he talks a little but is incontinent of urine and feces.

The patient's statement that he had felt guilty immediately after the sex experience, and that this guilt had remained as a persistent undercurrent of pre-

2. This case is dealt with at length by W. Muncie (The Psycholeptic Attack in the Psychoses, Arch. Neurol. & Psychiat. 27:352 [Feb.] 1932).

occupation, points to the close relationship of the content and the mood, the two hospitalizations being made necessary by the periodic intensification and elaboration of the content and a strong depressive mood. The first illness lasted almost a year. The second has lasted two years, with more evidence of the fixation of content as peculiar ideas of reference and with slump in habits.

The father was alcoholic and unfaithful to his wife. His philandering was the cause of great hostility in the patient (who had more rigid ideals, but whose sex curiosity led him further astray).

CASE 3.—*A woman in an access of sexual desire pressed a pet dog against her body, with consequent persistent undercurrent of feelings of guilt, delusions of pregnancy, and fear of widespread sexual disaster to white women and children at the hands of Negroes. Panic, agitation, marked depression, and elaboration and systematization of delusions for about a year were followed by apparent social recovery. An uncomplicated pregnancy followed later. For ten years the content lay dormant; then occurred a photographic recurrence of the content as well as of the depression and panic, lasting four years, again with social recovery. Evidence of habit deterioration was lacking, the important feature being the great fixity of the paranoid delusional material acting in a strong affective setting.*

*History.*—This patient, aged 29, entered the clinic in August 1921, when agitated, depressed and panicky, with delusions that she was pregnant and was going to give birth to a dog, and that children were to be assaulted by Negroes because of her behavior. She had been married at 21 (1913), wanted a child but had never been pregnant.

In January 1921 the patient was sitting watching her dog when suddenly the impulse to have intercourse with the dog came to her. She pressed it to her naked body, with the thought that somehow she must have a baby. In May 1921 it was as if a voice said to her: "You're going to have a dog," and from that moment appeared simultaneously agitation, depression with suicidal urge, delusion of pregnancy, begging for operation, fear that children were to be assaulted by Negroes and panic. She remained in the hospital until February 1922 and left with doubtful insight into her illness but with excellent surface adjustment.

Shortly after going home she became pregnant and gave birth to a daughter, without complications. There is evidence that the content remained latent and was regarded lightly until February 1931, when all the old ideas flared up again; the patient was admitted in a very agitated, depressed and panicky condition. She thought she was going to give birth to a monster, that Negroes pointed her out; she heard them call her a bitch and thought they were going to rape all white women and children. She was sleepless and wanted to die. She remained in the hospital with little improvement for seven months and was then transferred to a state hospital. Her condition remained essentially unchanged for four years. At times she denied all preoccupations, probably to impress the physician with her desire to go home, and finally achieved good social adjustment on trips home. She was discharged on her own demand and six months later appeared well. At no time was there evidence of a slump in habits or of intellectual deterioration.

Her mother and one sister were nervous, and her father was alcoholic.

CASE 4.—*A woman had two illnesses of photographic similarity, with depression, agitation, feelings of guilt, self-condemnation and panic, and ideas that she was presided over by a white angel and the devil and that her husband was Christ and her daughter the Bride of Heaven. Depersonalization followed what was probably an equivalent of psycholepsy, when she "felt the soul leave the body." Each attack was precipitated by sex arousal and finding herself the object of an aggressive extramarital sexual advance. The rapidity of reversion in the second*

*illness to the exact details of the first makes it probable that the sex factors remained a persistent influence throughout adult life.*

*History.*—The patient, a woman aged 45, was brought to the hospital agitated, deeply depressed and depersonalized, with feelings of guilt, and that she was forsaken by God. The illness began in January 1933, when the patient, in a setting of hard work in advanced musical study, alone in a foreign country, found herself the object of a young man's infatuation and herself sexually stirred. She revealed her desire in letters to her husband, and subsequently became remorseful and self-deprecatory because she could have been such a woman as to be desired by another man. The full picture of agitated depression soon appeared. In March 1933 she had a "vivid dream" and began saying that "a white angel, the devil and I only know about it"; "I'm falling into a pit." These were the same phrases she had used in a previous illness, at the age of 24, which lasted from one to two years in a setting of sex arousal by a dissolute man just before marriage.

In the hospital she continued in "low spirits," self-condemnatory, agitated and suicidal, with brief panicky episodes and spoke of having no emotions whatever, of being forsaken by God. The content resolved about her own sins but became elaborated to include the reincarnation of Christ in her husband and her daughter, the Bride of Heaven, as a contrast to her own unworthiness. She said she was dead; she had felt her soul leave her body; the children were not hers; she was going to the penitentiary, and was now in purgatory. She felt that a patient at the hospital was trying to take her husband from her (a patient who herself believed she was destined to wed Christ and was continually looking for him in the ward).

Three years after the onset the condition is worse, the content more fixed and the affect strongly depressive.

The patient's young daughter has just passed through a first depression in a similar setting of sex arousal and with somewhat similar content. One sister was depressed for a year at 35 through some sex maladjustment, which is not better differentiated.

Case 5 illustrates the influence of persistent content in a phasic affective reaction, and in this regard it is somewhat unusual.

*CASE 5.—A woman who hated her snobbish, brutal husband had a one-sided love affair with a casual acquaintance and reacted with depression to her inability to marry him. Five years later, "relieved" by her husband's sudden death, she became elated and planned to marry this acquaintance. Since then, periods of typical depression have alternated with periods of elation, without intervals of normality, always under the persistent influence of the one-sided love affair.*

*History.*—This patient, aged 50, chafing under marriage to a brutal, socially superior husband, childless, at 40 fell in love at first sight with an officer in an investment house handling her securities. This was a one-sided quasi-autistic affair, the man being totally unaware of it. The patient wanted to marry him and made plans to do so but was dissuaded by friends, whereon she reacted with typical depression which lasted several months. She then remained apparently well until her husband's sudden death with pneumonia five years later; she then immediately "felt relieved," and rapidly went into manic excitement, one feature of which was planning her wedding to the man she loved. This excitement, of about six months' duration, was followed by a depressive phase for from eight to ten months, with suicidal ruminations and ideas that people were stealing from her and were trying to get rid of her. A year later, without any interval of normality, she became elated again and now, after eight months, is still elated, with over-

activity, rhyming, punning and flight of ideas, declaring she is to marry the man; previous to hospitalization she had bombarded him with love letters and on one occasion demanded, to his astonishment, that he divorce his wife immediately and marry her.

The fixity of the underlying drive to marry this man carries a significance beyond that of the general increase in erotic activity attributable to the elation. It appears to have exerted a persistent influence, at times being manifested with depression and hopelessness over the situation, at others with characteristic manic push and determination. Insight has been totally lacking.

A half-brother committed suicide in a second attack of depression. The father was a stern Puritan but drank a great deal; the mother was high strung and held grudges. A maternal great-aunt had a "breakdown" at the time of the menopause, and another maternal cousin was "childish all her life."

#### SUMMARY OF CLINICAL FINDINGS

The clinical material may be summarized under the headings of the mental status:

*General Behavior.*—This shows the characteristics observed in states of tension, with restlessness, irritability and agitation or preoccupation or reduced activity (even to stupor). The diurnal variation in activity shows no constant pattern.

*Stream of Thought and Talk.*—There is constant harping on set topics, with typical depressive slowing, blocking or narrowing of the stream of talk by preoccupations, and sometimes with forced associations revolving about the content. There is seen in contrast a surprising ability to carry on even lively conversations on neutral topics.

*Mood.*—This is topically determined, with expressions of depression and hopelessness, such as "no future" and "damned," with suicidal preoccupations or with the more projected affect of hate, resentment and anger. There is no constant type of diurnal variation. Typical phasic affective reactions are possible. Depersonalization may be considered an equivalent of the mood. Expression of the mood is obtained only when the content is in the foreground; it is absent when neutral topics are mentioned. This should not mislead one as to the risk that the patient will attempt suicide.

*Content.*—There is harping on a set topic with a fixity which can amount to delusion and paranoid crystallization. The content constitutes a complex or a unit of concern of a type which superficially admits of no construction other than that which the patient has placed on it. Something has happened bringing unchangeable catastrophic consequences. Conviction of a physical change in the brain was included in one case. The type of the content will be referred to later.

*Special Features.*—These characterize such complex-determined reactions and constitute in themselves special content material through their importance in the evolution of the illness. They are: psycholeptic attacks and panics and their sequelae, especially depersonalization, ambivalence, blocking, forced associations and attempts at suicide. Such special episodes and symptoms are characteristic of states of prolonged tension and have in part been dealt with in previous communications.<sup>3</sup>

3. Muncie, W.: Depressions with Tension: Their Relation to the General Problem of Tension, Arch. Neurol. & Psychiat. 32:328 (Aug.) 1934. Muncie.<sup>2</sup>

Such features are commonly referred to in diagnostic terms as schizophrenic, so that a common diagnosis in such cases is "depression with schizophrenic features." It seems closer to the facts to attribute such incidental features to tension and its release (the tension in turn arises from the content in a setting of depression), without denying the ultimate possibility of a disorganization of personality and paranoid delusional fixation.

*Sensorium and Intellectual Resources.*—These are intact in the cases reported here. Examination is interfered with by blocking through preoccupation or by apathetic disinterest, difficulties of depressive thinking or ambivalence.

*Pattern of the Personality.*—Reactions of the type described occur in reticent sensitive persons who are rigidly uncompromising when their own set ethical and sex standards are concerned, unable to give credit to extenuating circumstances; or in persons with set ideas of what they expect from life who cannot brook disappointment or limitation from new responsibilities; in people who tend to hang on to, and elaborate on, topics of special concern, unable to make finished business in a socialized fashion of such topics, and who may react semi-automatically with ambivalence and contrast reactions of no longer affective plasticity.

*Physiologic Findings.*—These include the usual developments of depression, without, however, their ordinary global amelioration: anorexia, loss of weight, constipation, insomnia (of the "pure depressive" type, with early morning waking, or of the "impure depressive" type, i. e., with difficulty in falling asleep and sleepless nights, the result of a content disturbance of the fear or hate type) and loss of sex desire and interest (sometimes with episodic increase in sex desire). These are the usual findings in any prolonged state of tension with depression.

*Family History.*—About half the cases here described showed direct hereditary depressive tendencies in ancestors or in descendants. There were no deteriorative psychoses in the families. The material is too small to permit one to draw any conclusions concerning the significance of hereditary factors.

#### COURSE OF THE ILLNESS

Since reactions of the type described exhibit equally strong affect and content disturbances, each dependent on the other, a number of theoretical possibilities as to the outcome of such illness are presented, which conform also to the clinical facts.

The most favorable outcome is attained when the affect is strong and carries the content along with it. In such cases the content disturbance subsides as the depression recedes and "terminates" with the latter. As has been noted in connection with the recurrent attacks, this may be more an apparent than a real cure, if the content is still present in a latent or "walled off" form. This will be mentioned later.

A less favorable outcome is to be observed in cases in which the strength of the affect recedes, leaving the content in a commanding position and leading to strong paranoid delusional fixation. Even here, however, social rehabilitation of the patient may be possible, the content being present as undigested preoccupations but not operative

to any hindering degree. In this respect the patient resembles any paranoid person in whom strong affective features are lacking. Such a patient may show good preservation of personality, or he may never reach his former level of efficiency and may show striking alterations in personality after the first attack.

Another theoretical possibility is the development of an empty schizophrenic reaction through the recession of both the affect and the content, taking with them the bulk of the sustaining assets. This appears to have happened in many acute schizophrenic developments in young persons in whom strong affect and content reactions subsided quickly, leaving the patient totally apathetic and resistant to any attempt to regain normal activity, because of hypochondriacal complaints. There have been two such patients at this clinic recently; the initial experience had been depression in a setting of sex disappointment, followed by overactivity of a typically hypomanic character, then scattering, the formation of delusions and paralyzing apathy.

The prognostic possibilities include therefore: (1) the affect becoming dominant and carrying the content with it; (2) fixation of the content in a paranoid or disorganizing fashion, the mood receding; (3) recession of both mood and content, leaving emptiness and apathy.

Treatment may modify the outcome to a considerable degree.

#### THE TYPE OF CONTENT AND THE NATURE OF THE COMPLEX

In all the cases in this study a content was shown that was pre-eminently sexual; in the first patient the disturbance arose with the birth of the first child; in two, following sex experiences with animals in an attempt to substitute the experience for an unfulfilled desire (for pregnancy or for intercourse); in one, with sex arousal of a sort which she could not feel was ethically permissible, and in one, in the pursuit of a lover who meant a release from the bondage of marriage.

The first case was notable for the precipitating factor, namely, the birth of the first child, which was the result of parental urging, the baby being frankly unwanted on arrival. In this case there is no denial of the fact of the birth but an insistent demand that the episode be expunged from the record as peace could come only if the child were never to have been born, i. e., a demand that time itself be obliterated.<sup>4</sup> (A patient whom we saw in consultation recently showed

4. This case might be considered a prototype of the group studied by Zilboorg in thirty men and twenty-six women (*Depressive Reaction Related to Parenthood*, Am. J. Psychiat. **10**:927, 1931). He used the classic Freudian analysis. He summarized the findings in the female patients as follows: "On the whole, one might say that the trends in women center more definitely around the child than those in men, and that the formal picture of the depressive reactions in women shows a greater variety of deviations than that in men. The formal picture in men has more frequently a paranoid coloring and the suicidal drive appears to be stronger, while the depressive reactions in women run the whole gamut—from severe hysteroid or general psychoneurotic depression to mild schizophrenias." Aso, ". . . the woman who . . . wants to deny her motherhood finds herself in a much more difficult psychological situation than the man who wishes to deny his fatherhood. The man can escape into a paranoid trend, deny that he is the father of the children,

complete denial of motherhood with the arrival of a boy when a girl was wanted.)

It seems clear that the young woman in case 1 was or wanted to be carefree and playful and had entered into marriage with a poor conception of what the opportunities and responsibilities in the formation of the family were, and that she took up additional responsibilities only under pressure, disliked the new arrangement and vented this dislike on the husband, the child and self in a peculiarly set, rigid and torturing depression.

In general, it may be said that the content arises from conflict between crude strivings of personality and set ideals of personality. This conflict is predominantly, but not always, sexual, and in these patients involved adventuring of one sort or another which brought with it a sense of responsibility beyond that which the patient was able to bear in comfort, i. e., in conformity with his ideals and his habitual needs, likewise a responsibility which could not be denied in fact, whatever the extenuating circumstances. The psychosis was precipitated when the extenuating circumstances seemed to lose their validity in an increasing sense of guilt or unrest and fear; or when the life of new responsibility suffered increasingly in comparison with the former ease and freedom, and no amelioration was at hand.

#### DIAGNOSTIC CONSIDERATIONS

The reactions illustrated are affective reactions, arising directly from and best displayed with respect to certain topics of actuality, which it has been found difficult to incorporate adequately into the organization of the personality. Because of the strength of the affect factor (*thymos*) and of the equally great tendency to fixity and logical elaboration of the content (*nous*), such reactions might reasonably be called "thymonoic."

Thymonoic reactions are closely allied to catathymic depressions. Maier applied the latter term<sup>5</sup> to depressions (less often elations) in

and thus shift the responsibility for parenthood onto the shoulder of an imaginary lover of his wife. The woman, however, is prevented physiologically from denying the fact that the child is hers. The maximum flight from reality which she can achieve is to deny that she has ever been married and so insist that she is still a virgin, but even then it is impossible for her to deny the existence of her child, and hence we not infrequently find the trend in some young schizophrenic woman that the child has been conceived immaculately. It is therefore quite natural to expect that the pathological wish (conscious or unconscious) to get rid of the child whenever present must be greater in women than in men. . . ."

The case reported here was most inaccessible, and no statement is available concerning parent identification, incest wish and latent homosexuality.

5. The term catathymia (*Katathyme*) was first used by H. W. Maier (Ueber Katathyme Wahnbildung und Paranoia, Ztschr. f. d. ges. Neurol. u. Psychiat. 13: 555, 1912) to denote the workings of a fear, a wish or an ambivalent striving strong enough to disturb the balance between logic and affectivity and leading to "unusual and rigid combinations of associations which hang together in thought." He applied the term widely and believed that paranoia, as understood by Bleuler, represented the purest culture of the condition. Because of the wide application

(Footnote continued on next page)

which the affect is practically elicitable only in connection with certain topics on which the patient harps.

Recently a case was encountered at this clinic. A German housewife of 51 was examined whose only spontaneous complaint was that she suffered from an uncomfortable sensation in the throat, the result of swallowing a piece of lemon peel. Only very careful questioning and observation of her behavior disclosed the presence of "blueness," tearfulness and tension in connection with her complaint. The precipitating episode occurred at a time when she was much concerned over her son's recurrent drinking. Another patient gave as her complaint that her glasses did not fit; she had had them changed fourteen times within a few weeks. Here again in eight months of hospitalization frank depression was rarely observed, but rather the symptoms of a state of tension.

The reactions in the present series of cases are similar to catathymic depressions in the presence of definite topics and the centering of the affect about them, but they differ in (1) the obvious strong affect and (2) the nature of the topics (actualities acceptable to the personality with difficulty, some of many years' duration, with exacerbations to the point of clinical recognition from time to time).

These reactions are also allied to Wernicke's depressions with dominant ideas (*überwertige Ideen*), but later research into the concept of the *überwertige Idee* has left rather unclear and contradictory conclusions, in which the factor of mistake or misconception (*Irrtum*)<sup>6</sup> seems of considerable importance, at least as regards therapy and prognosis. The relation to delusion and to obsession is not clear. In the present cases the actuality of the factors must be stressed.

#### TREATMENT

Treatment of thymonoic reactions is difficult because the problems of the affect and content are both present; these are very active and interrelated, with a varying degree and type of plasticity or lack of it. Supportive treatment and distributive analytic-synthetic procedure with careful study of the personality are the usual means at hand. It becomes a matter of medical judgment when to stress one or the other, how fast to proceed with the study of the personality and when to give it up. Since study of the personality is apt to reveal what the patient is likely to view only in a self-derogatory fashion and so to increase the depression, great caution is necessary. Usually a study of personality can be attempted only when the physiologic and psychobiologic evidences of depression have been ameliorated. If analysis of the factors at work brings an exacerbation of the depression, a therapeutic rest is indicated. Sometimes, however, clearing of the depression is possible only with vigorous analysis of the dynamic factors at work. In any case and however deeply the study is able to proceed, it is the duty of the physician to see that the material so treated is left in the fashion most acceptable to the patient. It is manifestly unfair to unravel life experience and traits of personality before the eyes of a patient who

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of the term to states in which the affect factor is of doubtful importance, its usefulness has been somewhat invalidated.

6. Jahrreiss, W.: Ueberwertige Idee, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1928, vol. 1, no. 1, p. 581.

can view these features only in their most depressively derogatory character. If there are extenuating circumstances, as there always are, these must be pointed out without drifting into an irresponsible *laissez faire*. If the patient remains fixed in his thymonoic rut because of rigidity of personality, a glimpse of the workings of that rigid personality in a less fateful setting may help the patient to obtain an objective view of himself. For example, a patient recovering from a severe depression found his complete recovery blocked by the fact that his dramatic attempt at suicide spelled chagrin for him on his return home. The patient gained considerable help from the memory of how he used to suffer chagrin when as an usher in church he would find himself deserted by the communicants whom he thought he was ushering to a pew. This memory helped to deflate the importance of the attempt at suicide as such and placed the onus on a trait of personality, namely, his desire for the esteem of the community and his fear of appearing ridiculous. Treatment may be carried on by the help of the most simple expedients, demanding a healthy opportunism and the keeping always in mind that the patient has need of a more plastic and optimistic attitude toward himself and his living. Treatment which can make no compromises with reaching the ultimate in psychologic depth has no place here in spite of one's natural curiosity to know what is "behind it all."

Perhaps in many cases the most important point is to know when to stop in the study of the personality. When that time comes, early or late, the next procedure is to attempt to mobilize in the patient the overt assets which have sustained him in the past and to discover latent assets for use in the future. Many patients who can never make any constructive use of a study of the personality and in whom the content remains unchanged eventually reach the point where they are willing to try a cautious return to more useful living; in fact, they may demand it against medical judgment. Since thymonoic depressions are so grounded in the personality, it is asking a great deal that a personality "about-face" in the short term of hospital treatment. Nevertheless, the patient is always changing, and a new orientation to self and to life may be initiated in the hospital, which may need a considerable time to come to fruition. Contact with the patient after he has been returned to a semblance of his old life (or a better one) may aid him over many barriers, but generally only if it is sought by the patient.

Early discharge, as soon as the risk of suicide is gone and when good working rapport is established, is recommended, provided this will furnish contacts favorable to a proper life. This is especially true when the problem of the content seems to be untouchable but some return of former interests is shown.

The treatment may be said to resemble dissolution of the content or walling it off. The former means it has been absorbed in a healthy fashion into the body of the personality through the process of socialized thinking and affective acquiescence; the latter, that a truce is declared between the content and the body of the personality through the minimizing of the content in competition with more healthy bids for the patient's interest. Experience at this clinic shows the usefulness of both procedures, separately or in combination. An important need is

for the physician himself to remain plastic and not fall into the error of either perfectionism or mere license, which too often is the curse of the patient himself.

Experience shows these reactions to have a long chronic course, which is not to be wondered at in view of their origins. Nevertheless, social recovery has taken place in one case after four years' hospitalization and at a time when every one felt very dubious over the outcome.

#### SUMMARY

Clinical examples of reactions with coincidental and coeval strong affect and content fixation are not uncommon. They may be called thymonoic reactions.

The affect arises in connection with preoccupation over certain actual episodes or states integrated with difficulty into the organization of the personality.

The illness is long and difficult of treatment. The outcome varies, with the final emergence of the one or the other factor as dominant, or with the recession of both, leaving empty apathy.

## Technical and Occasional Notes

### STAIN FOR MYELIN SHEATHS IN TISSUES EMBEDDED IN PARAFFIN

GEORGE S. MAHON, M.D., NEW HAVEN, CONN.

Although methods for staining myelin sheaths in material embedded in paraffin have been described,<sup>1</sup> there has not been found in the literature to date a technic that does not require differentiation. In working with the modification of the Pal-Weigert stain described by Clark and Ward,<sup>2</sup> it was observed that their method, when applied to sections embedded in paraffin, resulted in a selective stain of the myelin sheaths.

The material on which this stain has been used was obtained at autopsies performed as a routine by the department of pathology of the Vanderbilt University Hospital. None of the material was specially selected. The time that elapsed between death and autopsy varied from one to fourteen hours.

#### REAGENTS

1. Four per cent solution of iron alum (iron and ammonium sulfate) in distilled water. This may be made up in bulk and kept indefinitely, until needed, or a 40 per cent solution may be made and diluted as needed.
2. Saturated solution of lithium carbonate in distilled water. This can be kept indefinitely in bulk.
3. Ten per cent solution of hematoxylin<sup>3</sup> in absolute alcohol. This can be made up in quantities large enough to last three months, or longer if desired. The solution does not need ripening and is ready for use as soon as prepared.

#### TECHNIC

1. Fix thoroughly in bulk in a 10 per cent dilution of formaldehyde U. S. P. Commercial formaldehyde, either unneutralized or neutralized with calcium carbonate, is satisfactory. Material that had been in formaldehyde for a year has stained fairly well, but best results have been obtained with material embedded as soon as possible after thorough fixation. With the spinal cord, blocks can be cut and put in the dehydrating alcohols within forty-eight hours after the material has been placed in formaldehyde.

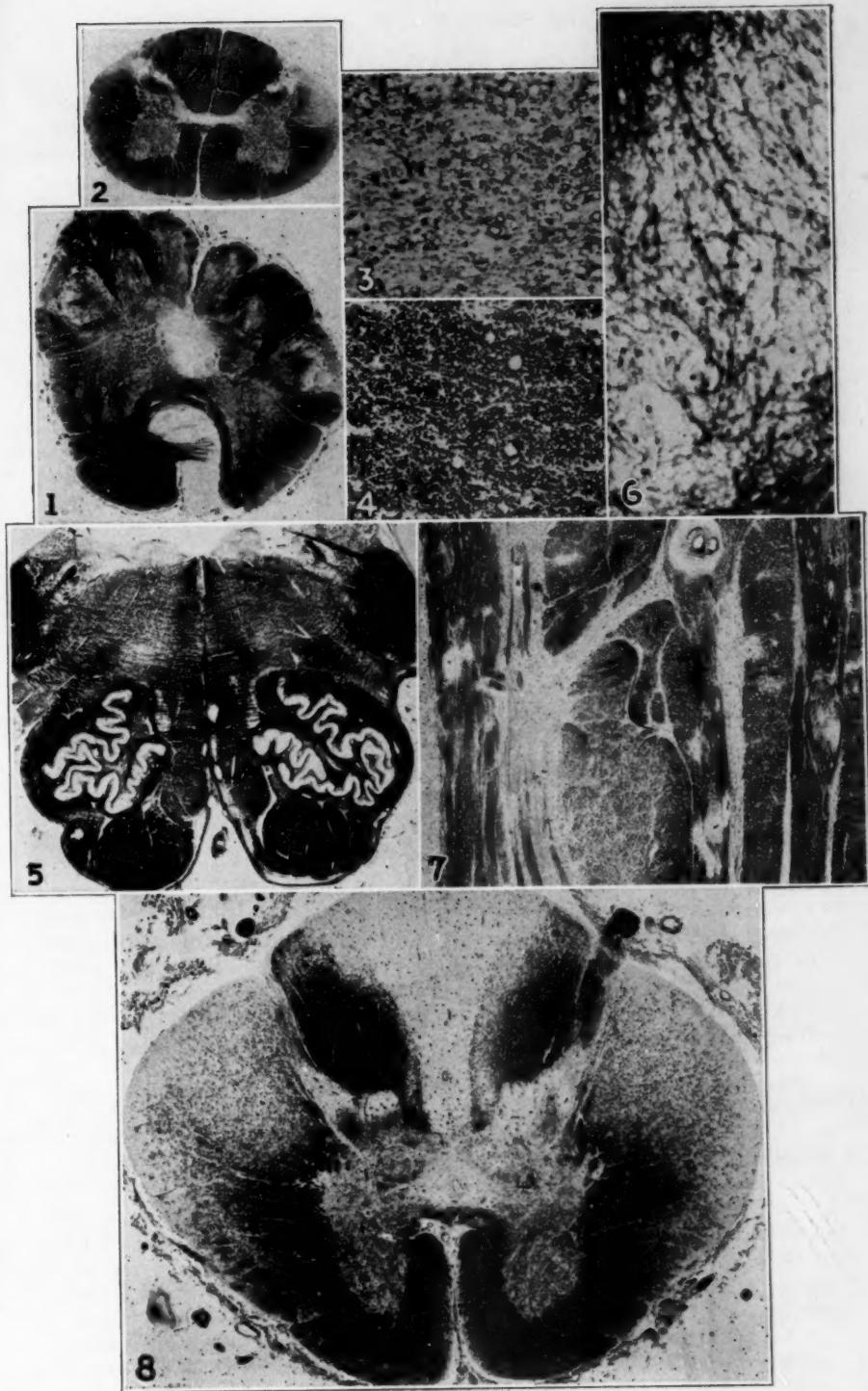
From the Department of Pathology, the Vanderbilt University School of Medicine, Nashville, Tenn.

1. Weil, Arthur: Rapid Method for Staining Myelin Sheaths, *Arch. Neurol. & Psychiat.* **20**:392 (Aug.) 1928. Gozzano, Mario: *Boll. d. Soc. Ital. di Biol. sper.* **4**:1219, 1929.
2. Clark, S. L., and Ward, J. W.: *Stain Technol.* **9**:53 (April) 1934.
3. The hematoxylin was secured from Coleman & Bell Company, Norwood, Ohio.

EXPLANATION OF PLATE

Photomicrographs of sections stained for myelin sheaths: 1 shows degeneration of the left pyramidal tract at the decussation,  $\times 4$ ; 2, the level of the lumbar portion of the cord,  $\times 4$ ; 3, detail from the area of the degenerated right lateral corticospinal tract,  $\times 100$ , and 4, detail of the normal corticospinal tract area on the left,  $\times 100$ . 1, 2, 3 and 4 are taken from paraffin sections in the same case. 5 shows a section of the normal cord (pyroxylin;  $\times 4$ ), and 6, a detail from the olive in the section illustrated in 5, demonstrating the thorough staining of the fiber net work (pyroxylin;  $\times 250$ ). 7 shows multiple perivascular foci of demyelination in a case of hypertensive nephritis with heart failure (paraffin;  $\times 19$ ), and 8, the thoracic portion of the cord, just above the level of compression by an extradural hemangioma, of several years' duration (paraffin;  $\times 14$ ).

All paraffin sections were 12 microns thick, and the pyroxylin sections, 34 microns thick.



PLATE

2. Embed in paraffin according to the usual technic. Cut sections from 6 to 18 microns; mount on slides with albumin and glycerin; deparaffinize, and run down to water.<sup>4</sup> It is recommended that the xylenes and alcohols for deparaffination in this procedure be kept apart, and not used with any except formaldehyde-fixed tissue.

3. Mordant for from fifteen to thirty minutes in a 4 per cent solution of iron alum at room temperature.

4. Rinse two or three times in distilled water.

*Caution.*—The rinsing must be thorough, but not prolonged. Half a minute is long enough.<sup>5</sup>

5. Stain for from thirty to sixty minutes in lithium carbonate-hematoxylin, made by adding 1 volume of solution A (10 per cent solution of hematoxylin in absolute alcohol) to 9 volumes of solution B. Solution B is prepared by diluting 7 cc. of a saturated aqueous solution of lithium carbonate to 100 cc. with distilled water. The solutions must be mixed fresh each time before using. Stain that has been used once or that has stood for some hours has not given desired results. The number of slides to a staining dish is not limited, if the stain covers each section completely.

The time allowed for mordanting and for staining is that minimal for good results. Experience with the technic indicates that it is not possible to over-mordant or over-stain within reasonable time limits, i. e., from twelve to twenty-four or forty-eight hours, for the mordant, and from two to six or eight hours, for the stain.

6. Wash in either distilled or tap water to remove excess stain.

7. Leave in a saturated solution of lithium carbonate for from fifteen to thirty minutes to blue the myelin sheaths.

8. Wash thoroughly. Dehydrate in 95 per cent and absolute alcohol. Clear in xylene. Mount in neutral xylene balsam.

#### RESULTS

The myelin sheaths are sharply and distinctly stained deep blue or blue black. The background is white and colorless. Red cells and nucleoli are black. If the sections have been washed too long between the mordant and the stain, the nerve cells and glia nuclei are stained faint brown or black, and Nissl granules may be indicated.

The same technic has been applied to pyroxylin sections, from 20 to 40 microns thick, with good results.<sup>6</sup> The only difference noted is that

4. Thicker sections have been found to give a more satisfactory preparation for examination with the naked eye or with a hand lens.

5. Too long rinsing will result in an undesirable yellowish brown tone of the background. The tap water at Nashville has been as satisfactory as distilled water for rinsing, but tap water elsewhere might not do as well.

6. Blocks for embedding in pyroxylin are passed through 70 and 80 per cent alcohol, two jars each of 95 per cent alcohol and absolute alcohol, a mixture of absolute alcohol and ether (equal parts) and 4, 8 and 14 per cent solutions of pyroxylin made by dissolving nitrocellulose (pyroxylin), type 7,113 (Du Pont de Nemours and Company), in equal parts of absolute alcohol and ether. The blocks are left in the alcohols and solutions of pyroxylin from one to four days, depending on their size. The block is mounted from the 14 per cent pyroxylin and immediately immersed in chloroform, where it stays until the pyroxylin is sufficiently hard. Then the mounted blocks are stored in 80 per cent alcohol until they are cut.

in pyroxylin sections there is a tendency for the gray matter to take a bluish tone, undesirable in a background.

Attempts to apply this technic to frozen sections have not been successful.

Good results have been obtained with all material subjected to this technic, except a spinal cord that had remained in alcohol for a long time. The method does not give results with the cortex that would make possible a study of the cortical myelo-architectonics. At all lower levels, however, the myelin has stained well, and the demonstration of demyelinating lesions has been excellent.

The duration of the stay in the saturated solution of lithium carbonate after staining seems to be important for bringing out fibers that are not apparent when the excess of stain is first washed off and for converting the original black of the fibers into deep blue. Sections that have stained for only fifteen minutes will give an adequate picture, if the subsequent stay in lithium carbonate is prolonged. Curiously, the shorter the staining period, the greater appears to be the tendency for the background elements to be stained, and in a section stained for fifteen minutes the nuclei take an excellent blue stain, with the nucleoli a deep blue black.

Other methods have been described<sup>7</sup> for selective staining of myelin sheaths without preliminary mordanting of the block or differentiation of the sections after staining. Both these methods employ modifications of the principle of the fat stain and consequently demand frozen sections for success. Except for the single factor of speed, the paraffin section method recommends itself over these methods by reason of its adaptability to the routine for paraffin sections in use in general pathologic laboratories, its fitness for studies of serial sections and the permanence of the preparations obtained.

#### SUMMARY

A technic is described for selective staining of myelin sheaths in formaldehyde-fixed, paraffin-embedded material. This technic does not require mordanting of the blocks of tissue prior to embedding, nor does it require differentiation of the sections after staining. It is believed that the simplicity and relative rapidity of the technic, the lack of rigid time requirements and the uniformity of results make the method of value, particularly for use as a routine in a laboratory of general pathology.

The technic is applicable to pyroxylin-embedded material, but not to frozen sections.

7. Lison, L., and Dagnelie, J.: Bull. d'histol. appliq. à la physiol. **12**:85, 1935.  
Landgraf, Gabriele: Centralbl. f. allg. Path. u. Anat. **63**:56, 1935.

## SPECIAL ARTICLES

### UNILATERAL CEREBRAL DOMINANCE AS RELATED TO MIND BLINDNESS

MINIMAL LESION CAPABLE OF CAUSING VISUAL AGNOSIA  
FOR OBJECTS

J. M. NIELSEN, M.D.  
LOS ANGELES

The concept of unilateral cerebral dominance originated with Marc Dax,<sup>1</sup> who in 1836 published the observation that hemiplegia affecting the right side of the body is far more often associated with loss of speech than is a similar paralysis of the left side. Through the work of Broca,<sup>2</sup> Troussseau,<sup>3</sup> Wernicke,<sup>4</sup> Kussmaul,<sup>5</sup> Jackson<sup>6</sup> and Bastian,<sup>7</sup> to mention only a few of the most prominent pioneers in the study of aphasia, the dominance of the major (usually the left) side of the brain over the minor side in speech was soon established, so that this is now common knowledge.

With the work of Liepmann<sup>8</sup> on apraxia, a similar dominance for voluntary acts became recognized to some extent, but several

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Read before the Section on Nervous and Mental Diseases at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 15, 1936.

1. Dax, Marc: *Lésions de la moitié gauche de l'encéphale coïncidant avec l'oubli des signes de la pensée*, Montpellier, 1836.
2. Broca, P.: *Perte de la parole. Ramollissement chronique et destruction partielle du lobe antérieur gauche du cerveau*, Bull. Soc. d'anthrop. de Paris **2**:235, 1861; *Nouvelle observation d'aphémie produite par une lésion de la moitié postérieure des deuxièmes et troisième convolutions frontales*, Bull. Soc. anat. de Paris **36**:398, 1861; *Remarques sur le siège de la faculté du langage articulé avec deux observations d'aphémie*, ibid. **36**:330, 1861.
3. Troussseau, A.: *De l'aphasie*, in *Clinique médicale de l'Hotel-Dieu de Paris*, ed. 7, 1862.
4. Wernicke, C.: *Der aphasische Symptomcomplex*, Breslau, M. Cohn & Weigert, 1874.
5. Kussmaul, A.: *Die Störungen der Sprache. Versuch einer Pathologie der Sprache*, ed. 3, Leipzig, F. C. W. Vogel, 1885.
6. Jackson, J. Hughlings: *Selected Writings*, London, Hodder & Stoughton, 1932, vol. 2, pp. 146-211.
7. Bastian, H. C.: *Ueber Aphäsie und andere Sprachstörungen*, German translation by Moritz Urstein, Leipzig, Wilhelm Engelmann, 1902.
8. Liepmann, H.: *Das Krankheitsbild der Apraxie (motorische Asymbolie)*, Monatschr. f. Psychiat. u. Neurol. **8**:15, 102 and 182, 1900; *Der weitere Krankheitsverlauf bei dem einseitig Apraktischen und der Gehirnbefund auf Grund von Serienschnitten*, ibid. **17**:289, 1905; **19**:217, 1906.

investigators, notably von Monakow<sup>9</sup> and his pupil Brun,<sup>10</sup> have taken exception to this doctrine as originally outlined.

For general sensation it is established beyond question that there is no such dominance, astereognosis, which is tactile agnosia, occurring unilaterally from a lesion in either parietal lobe. With respect to the special senses of taste and smell, one is still unable to differentiate between peripheral loss and agnosia. With regard to hearing, unilateral dominance for interpretation of sounds heard is part of aphasia and, as already stated, is clearly lateralized to the major side. The problem whether similar cerebral dominance applies to elaboration of visual perception has occupied the minds of notable investigators. Wilbrand,<sup>11</sup> Gowers,<sup>12</sup> Oppenheim,<sup>13</sup> Heilbronner,<sup>14</sup> Lissauer,<sup>15</sup> Pötzl<sup>16</sup> and von Monakow<sup>17</sup> are particularly to be mentioned. The article of Rabus<sup>18</sup> was valuable, and the monograph of Nodet<sup>19</sup> was a distinct contribution, containing abstracts of a great many cases from the literature. Henschen,<sup>20</sup> in his notable monograph on aphasia, in which he abstracted nearly 1,500 cases, in most of which there was verification at autopsy, noted the presence of mind blindness (*Seelenblindheit*) whenever it was present but did not take up the question discussed in this paper. He

9. von Monakow, C.: *Gehirnpathologie*, ed. 2, Vienna, Alfred Hölder, 1905.

10. Brun, R.: *Klinische und anatomische Studien über Apraxie*, Zurich, Art Institut Orell Füssli, 1922.

11. Wilbrand, H.: *Die Seelenblindheit als Herderscheinung und ihre Beziehungen zur homonymen Hemianopsie, zur Alexie und Agraphie*, Wiesbaden, J. F. Bergmann, 1887.

12. Gowers, W. R.: *A Manual of Diseases of the Nervous System*, ed. 1, London, J. & A. Churchill, 1888, vol. 2, pp. 102-117

13. Oppenheim, H.: *Die Störungen der Sprache*, in *Lehrbuch der Nervenkrankheiten für Aerzte und Studierende*, ed. 3, Berlin, S. Karger, 1902.

14. Heilbronner, K.: *Die aphasischen, apraktischen und agnostischen Störungen*, in Lewandowsky, F.: *Handbuch der Neurologie*, Berlin, Julius Springer, 1910, vol. 1, pp. 982-1093; *Ueber isolierte apraktische Agraphie*, München. med. Wchnschr. **53**:1897, 1906.

15. Lissauer, H.: *Ein Fall von Seelenblindheit nebst einem Beitrag zur Theorie derselben*, Arch. f. Psychiat. **21**:222, 1889.

16. Pötzl, O.: *Die Aphasielehre vom Standpunkte der klinischen Psychiatrie*, Leipzig, Franz Deuticke, 1928, vol. 1.

17. von Monakow, C.: *Die Lokalisation im Grosshirn und der Abbau der Funktion durch kortikale Herde*, Wiesbaden, J. F. Bergmann, 1914.

18. Rabus, H.: *Zur Kenntnis der sogenannten Seelenblindheit*, Erlangen, F. Junge, 1895.

19. Nodet, V.: *Les agnosies; la cécité psychique en particulier*, Thèse de Lyon, no. 2, 1899.

20. Henschen, S. E.: *Klinische und pathologische Beiträge zur Pathologie des Gehirns*, Stockholm, Nordiska Bokhandeln, 1920-1922, vols. 5, 6 and 7.

stated that the greatest minds had already applied themselves to a solution of the problem.

A priori, it seems strange that visual agnosia for objects might be due to a unilateral lesion. Unilaterality of function seems definitely related to handedness and this in turn to the use of instruments. One might, then, expect unilaterality of function only in trained apes (if it can develop in the course of a lifetime) and in the human subject. The experiments of Munk<sup>21</sup> and Ferrier<sup>22</sup> on the dog and ape did not indicate any unilaterality of cerebral function for recognition of objects through vision. If, then, there is unilateral dominance or preponderant unilaterality of function in one occipital lobe in man, one must assume with Mingazzini and S. D. Ingham that as one side has become dominant in speech and in voluntary motor acts, the patterns for visual memory are laid down on the same side for closer association with speech and motor mechanisms.

I shall quote what masters of the subject have stated concerning the site of the lesion capable of causing mind blindness and then indicate a possible cause of the discrepancy of opinion and the feasibility of solution through subdivision of the problem.

Gowers<sup>12</sup> said:

The structures that subserve the functions lost in mind-blindness are certainly separate from those of the half-vision centers, since hemianopia from disease of the cortex does not necessarily involve this special loss. The centers concerned are probably in front of the half-vision region, either in the anterior part of the occipital lobes or in the posterior part of the parietal lobes. The latter is more probable. . . . We do not know whether complete mind-blindness can be produced by a lesion in one hemisphere, or whether disease of both hemispheres is necessary for the production of the symptom.

He then referred to the case of Chauffard<sup>23</sup> and that of Bernheim<sup>24</sup>; he explained mind blindness in the former on the basis that in such instances the condition is probably transient and in the latter on the ground of a previous lesion on the other side.

Mills<sup>25</sup> said:

The center for the visual images of things probably includes or is adjacent to that for visual images of words; but both hemispheres doubtless take part in the storage of object images, and in nearly equal degree; while for the recognition

21. Munk, H.: Ueber die Functionen der Grosshirnrinde, Berlin, A. Hirschwald, 1881; cited by Luciani and Seppelli.<sup>47</sup>

22. Ferrier, D.: The Function of the Brain, ed. 2, London, Smith, Elder & Co., 1886.

23. Chauffard, A.: Rev. de méd. 1:940, 1881.

24. Bernheim: Rev. de méd. 5:625, 1885.

25. Mills, C. K.: The Nervous System and Its Diseases, Philadelphia, J. B. Lippincott Company, 1898.

of words, as for the other higher faculties, man is mainly left-brained. A few cases of partial mind-blindness are on record in which unilateral lesions were present.

Oppenheim<sup>18</sup> in 1902 and again in 1913 said (in referring to a diagram):

If the fibers *O.W.* are destroyed on the one side and the fibers *O.E.* or the tract *F* on the other (fiber tracts corresponding to the transverse occipital fasciculi of Sachs and Viallet), unilateral hemianopia and mind blindness results.

This is equivalent to saying that if the paths from the right occipital lobe and those from the left calcarine area to the left occipital cortex are destroyed at the same time, unilateral hemianopia plus mind blindness results. (Henschchen<sup>20</sup> made the same suggestion in 1922.)

Monakow<sup>19</sup> in 1905 said:

Concerning the more exact anatomic conditions necessary for the development of mind blindness, it is possible to make only the following statement on the basis of the material available: The disturbance can arise only when extensive, deep-lying, bilateral and, when possible, symmetrical lesions, especially in the lateral occipital convolutions, are present. . . . The more the lesion extends into the white matter from the cortex of the parieto-occipital area the more likely are the symptoms of mind blindness to appear. . . .

In 1914 he stated<sup>17</sup>:

In my opinion, pathologic observations, combined with the results of experiments to date, speak definitely for the following: The symptom complex of visual agnosia as a permanent condition does not have as its basis a localized anatomic defect, but there are manifold factors, and functional disturbances as well, in which interference with circulation plays an important rôle (page 483).

Heilbronner<sup>14</sup> said:

In spite of anatomic material, which already is abundant, it is still impossible, on the basis of the clinical manifestations of mind blindness alone, to reach with certainty conclusions concerning the extent of the causative lesion. . . . In the cases in which pathologic observations were made, severe mind blindness, especially if long continued, rests chiefly on the presence of bilateral lesions (which does not preclude considerable restitution, as in the case of Wilbrand). However, the number of cases in which there was a unilateral lesion, almost without exception on the left side, is now not inconsiderable.

Wilbrand and Sänger<sup>26</sup> said:

To summarize briefly, we can accept that visual agnosia occurs only in disease of the occipital lobe. Localization relative to exactly which part of the cortex or the white substance must be destroyed in order to provoke mind blindness we cannot give.

26. Wilbrand, H., and Sänger, A.: Die homonyme Hemianopsie, in Die Neurologie des Auges; ein Handbuch für Nerven- und Augenärzte, Wiesbaden, J. F. Bergmann, 1917, vol. 7, p. 425.

Mingazzini<sup>27</sup> said:

With regard to man, the question arises whether visual agnosia is dependent on a lesion of a single occipital lobe or of both lobes, and this question is still open. It is directly associated with the function of the splenium. As, according to pathologic experience, extensive lesions of both occipital lobes do not of necessity cause lasting forms of visual agnosia, it was assumed that lesion of one occipital lobe does not cause visual agnosia. However, this is not so (in contrast to the condition observed in the dog and in Macacus). In fact, it is established on the basis of numerous clinical observations that at times a disease focus in one occipital lobe, usually the left, is enough to cause signs of mind blindness, even of all degrees.

Pötzl<sup>16</sup> said:

Especially lesions of the left side at the base of the occipital lobe come into consideration in the solution of Lissauer's mind blindness, but only when (besides cortical disturbances of variable degree and extent) much of the white substance is destroyed and the splenium of the corpus callosum is severely affected.

Thiele<sup>28</sup> did not take up the question for his own solution but pointed to the case of Heidenhain<sup>29</sup> to prove that local lesion without general cerebral involvement was sufficient to cause mind blindness. (Heidenhain's patient, however, had bilateral occipital lesions.)

With this summary, it will be seen that Oppenheim, Henschen, Heilbronner and Mingazzini have pointed out that a unilateral lesion may cause mind blindness. However, investigators whose opinions cannot be set aside without careful scrutiny have taken the view that there must also be a lesion of some sort, either general or local, on the other side. I believe that this discrepancy is due to the lack of definition of terms.

#### DEFINITION OF TERMS

Visual agnosia for objects is loss of ability to identify objects by sight alone, sufficient acuity of vision and general cerebral function being present and the patient being still able to recognize the object in question through some other sensory channel. To clarify the matter it is necessary to give a historical introduction. Steinthal<sup>30</sup> used the term "asemia" (loss of ability to communicate by signs) to indicate the loss of capacity to comprehend or use signs. Finkelnburg<sup>31</sup> suggested

27. Mingazzini, G.: *Der Balken*, Berlin, Julius Springer, 1922, p. 184.

28. Thiele, R.: *Aphasie, Apraxie, Agnosie*, in Bumke, O.: *Handbuch der Geisteskrankheiten*, Berlin, Julius Springer, 1928.

29. Heidenhain, A.: Beitrag zur Kenntnis der Seelenblindheit, *Monatschr. f. Neurol. u. Psychiat.* **66**:61 (Oct.) 1927.

30. Steinthal: *Abriss der Sprachwissenschaft*, Berlin, 1871.

31. Finkelnburg: *Ueber Aphasie und Asymbolie, nebst Versuch einer Theorie der Sprachbildung*, *Arch. f. Psychiat.* 1876, vol. 6.

the term "asymbolia" to replace this. However, as Kussmaul<sup>31</sup> pointed out, "asemia" is more inclusive, for behind a sign there may be only a feeling while behind a symbol there is always an idea. "Asymbolia" therefore could not logically replace "asemia." Without careful analysis on the part of workers in the field "asymbolia" has, nevertheless, become established in the place formerly held by "asemia." Meynert<sup>32</sup> called the loss of identification signs of objects asymbolia. With the inclusion with these identification signs of the concept of the use of objects (a motor type of memory picture), the terms sensory asymbolia and motor asymbolia came into being.

In 1891 Freud<sup>33</sup> came to the rescue with the term "agnosia," which he proposed to represent the relation between object and object concept, arguing that "asymbolia" was a more proper designation for the relation between word and object concept. This was a salutary suggestion and was soon accepted, but there was still difficulty in distinguishing between apraxia and agnosia, for it was not discovered until 1900 (by Liepmann<sup>34</sup>) that apraxia is purely motor. After this agnostic disturbances were still confused with apraxia because erroneous use of objects might be due to lack of recognition; so the term agnostic apraxia arose. With the final distinction between the two that agnosia is sensory and apraxia motor, the term agnosia was established in the literature.

With this establishment there arose an intensive study of agnosia, and the complexity of even simple recognition was soon evident. Liepmann<sup>35</sup> spoke of primary identification, by which he meant (with reference to vision) the memory picture which is formed simultaneously with the visual image. By secondary identification he meant the combined concept obtained by associating with the visual memory picture the pictures obtained through the other senses. Later, on the basis of clinical cases, he suggested the terms dissolutive and disjunctive agnosias, by which he meant various forms of disturbed identification in the higher elaboration of the concept.

The term was further complicated by others. To Freud's original idea of agnosia for objects was soon added that of agnosia for pictures. Wolpert<sup>36</sup> then used "simultanagnosia," or the loss of ability to recognize processes (or action, as indicated in a still picture). This, carried

32. Meynert, T.: Ein Fall von Sprachstörung, anatomisch begründet, Med. Jahrb. **12**:152, 1866.

33. Freud, S.: Zur Auffassung der Aphasien, eine kritische Studie, Leipzig, Franz Deuticke, 1891.

34. Liepmann, H.: Ueber die agnostischen Störungen, Neurol. Centralbl. **27**: 609, 1908.

35. Wolpert, I.: Die Simultanagnosie (Störungen der Gesamtauffassung), Ztschr. f. d. ges. Neurol. u. Psychiat. **93**:397, 1924.

to its logical conclusion, brought up the loss of understanding of cinematographic images. A form stressed by various writers is the loss of revisualization of former images.

The term visual agnosia (at first applied only to loss of recognition of objects) has thus been broadened so that it is almost as inclusive as mind blindness. Many writers on cerebral localization as related to visual agnosia have considered the two terms almost identical and have studied mind blindness as a unit. How far afield one may be led by this loose designation may be gathered from the following list of "agnosias," the presence of any one of which has by various authors been considered sufficient evidence of the presence of mind blindness.

1. Visual agnosia for objects and pictures (Lissauer<sup>15</sup>).
2. Simultanagnosia (Wolpert<sup>16</sup>).
3. Amnesic color blindness (Wilbrand and Sänger<sup>17</sup>).
4. Apperceptive blindness of the senile (Pick<sup>18</sup>).
5. Disorientation in space.
6. Geometric-optic agnosia.
7. Psychic paralysis of gaze (Bálint<sup>19</sup>).
8. Loss of perception of distance.
9. Optic aphasia for objects and symbols.
10. Visual verbal agnosia.
11. Visual agnosia for letters or figures.
12. Visual agnosia for musical notes.
13. Subcortical visual verbal agnosia ("pure" visual verbal agnosia of Déjerine<sup>20</sup>).
14. Dissolutive, disjunctive and ideational agnosias (of Liepmann<sup>21</sup>).

The classification of such a heterogeneous gathering under one name must lead to confusion. Certainly, a small lesion cannot cause all these manifestations. From the standpoint of cerebral localization, it seems far more practical for an investigator to select a definite form for primary consideration and attempt to determine the site of a lesion which might be responsible for its production. In his monograph

36. Wilbrand.<sup>11</sup> Wilbrand and Sänger.<sup>26</sup>

37. Pick, A.: Zur Symptomatologie des atrophischen Hinterhauptlappens, in Arbeiten aus der deutschen psychiatrischen Universitäts Klinik in Prag, Berlin, S. Karger, 1908, p. 42.

38. Bálint, R.: Seelenlähmung des Schauens, optische Ataxie, räumliche Störung der Aufmerksamkeit, Monatschr. f. Psychiat. u. Neurol. **25**:51, 1909.

39. Déjerine, J.: Aphasic, in Sémiologie des affections du système nerveux, Paris, Masson & Cie, 1900, p. 394-469.

Pötzl<sup>16</sup> separated the subtypes of the form of Lissauer and gave the following conclusions:

While one should in no wise neglect the fact that diffuse destruction of the white matter may cause this condition, the question of which cyto-architectonic and myelo-architectonic regions of the occipital cortex are of the greatest importance to the systems damaged should, but cannot with certainty, be answered. First for consideration in any case comes area 18 of Brodmann, with its borders on areas 17 and 19.

Pötzl did not, however, present the material on which he based this conclusion. To verify this statement, if possible, is the purpose of this paper.

#### SELECTION OF CASES

Selection of cases from the literature for this investigation has been made according to the following rigid rules: 1. The record of the case as published not only must state that visual agnosia for objects was present but must offer evidence for scrutiny and independent diagnosis.<sup>40</sup>

40. This was done to eliminate several sources of error, particularly that of mistaking apraxia. In the case of Weissenberg (Weissenberg, S.: Ein Beitrag zur Lehre von den Lesestörungen auf Grund eines Falles von Dyslexie, Arch. f. Psychiat. **22**:414, 1890-1891) the author may have had evidence to prove visual agnosia for objects, but all the records of performance and of questions and answers which he furnished for scrutiny proved nothing but the presence of apraxia. The case of Liepmann (Liepmann, H.: Gehirnbefunde bei Aphasischen und Agnostischen, abstr., Berl. klin. Wchnschr. **52**:959 [Sept. 6] 1915) is also rejected for lack of evidence. I do not doubt the presence of "optic-tactile" agnosia, as the author stated, but this does not prove the presence of visual agnosia for objects. The case reported by Bernheim (Bernheim<sup>24</sup>: Contribution à l'étude de la cécité. Psychique des mots et des choses, Arch. de neurol. **36**:69, 1914) is not included because the sole proof of visual agnosia for objects was the observation that when he was asked to pick up a fork, knife, handkerchief, pair of scissors and keys, the patient often selected the wrong article. (Apraxia might account for this, especially as the author proved that apraxia was present.) Then, in the description of acoustic agnosia, which also was present, the author stated that he said to the patient: "Give me what I need to read" and "Give me what is necessary for eating," on which the patient gave him the appropriate book and fork. The patient must, therefore, have recognized objects. The case of Monakow<sup>17</sup> (page 526) has been abstracted by various workers as one of mind blindness. However, Monakow stated clearly that the patient recognized his environment; hence, he could not have been mind blind for objects. The case of Ide (Ide, C. E.: Psychic Blindness, Am. J. Ophth. **10**:516, 1927) was clearly not one of mind blindness. The diagnosis was based on a claim of blindness by the patient, in the presence of normal fundi. On this basis the author assumed visual agnosia. The case of Laquer (Laquer, L.: Localisation der sensorischen Aphasie, Neurol. Centralbl. **7**:337, 1888) is excluded because the patient was not clearly mind blind, certainly not for pictures. At first she had apraxia, but this disappeared before death. The case of Mills and McConnell (Mills, C. K., and McConnell: J. Nerv. & Ment. Dis. **21**:1 [June] 1895) has been cited as relevant to this subject. The authors stated clearly, however, that the patient was unable merely to name objects not to recognize them.

2. Only one occipital lobe must have been affected. It is clear that if in any case a unilateral lesion produced visual agnosia, there can be no point in citing cases of bilateral lesion of the occipital lobes.<sup>41</sup>

3. The lack of recognition of objects must not have been due to general cerebral involvement or enfeeblement.<sup>42</sup>

The case of Souques (Souques, A.: *Un cas d'alexie ou cécité verbale dit pure suivi d'autopsie*, Bull. et mém. Soc. méd. d. hôp. de Paris **24**:213, 1907) is rejected because the author stated that, while the patient was unable to name objects, he knew what they were and that, while he could not find his way about the room, allowance must be made for memory defect and hemianopia. This, then, was chiefly a case of visual aphasia, not of agnosia.

4. The agnosia must have been more than transient. If the patient recovered before death or if diaschisis seemed to have been the cause of the syndrome, the case was not included.<sup>43</sup>

5. The lesion must have been verified.<sup>44</sup>

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41. On this ground the case of Reinhard (Reinhard: *Beitrag zur Casuistik der von Fürstner beschriebenen "eigenthümlichen Sehstörung bei Paralytikern,"* Arch. f. Psychiat. **9**:147, 1879) is rejected. The patient had cysticercus of the brain, and the lesions must have been bilateral, even though they were observed only on one side. The case of Heilbronner (Heilbronner, K.: *Ueber Asymbolia*, Breslau, Schletter, 1897) is rejected because, according to the records, both angular gyri were affected. It is not clear whether the occipital lobes were free.

42. The case of Wilbrand and Sänger<sup>26</sup> (patient Trutzel) must be excluded on this basis. The patient had not worked for ten years and had not been able to read for two years; his thoughts were not clear; he was unable to recognize objects by touch, and speech was slurred and incomprehensible. Autopsy showed internal hydrocephalus arising from cerebral atrophy. The small lesion in the left third occipital convolution was not the sole cause of visual agnosia. It was only the final element causing an area of acute destruction in a site close to the cortical area which is specifically necessary for recognition of objects. (This will be shown later.) Niessl von Mayendorf (Klin. Wchnschr. **4**:451 [March] 1925) expressed the opinion that this case was a crucial one, proving his contention of the mechanism of mind blindness. It seems to me far from a clearcut instance.

43. Rejected on the basis of the condition being only transient are the following: (1) Case of Chauffard.<sup>23</sup> The patient lived only three days after the insult; even during this time he recognized some objects, as shown by the fact that he took his glass and sputum cup and that he knew the handle of the cord at the side of the bed. The edema of the acute lesion may easily have been the cause of the mind blindness which was said to have been present. This interpretation is supported by the fact that acoustic verbal agnosia was also reported, while the superior temporal convolution was not directly involved. (2) Case of Monakow (von Monakow, C.: *Experimentelle und pathologisch-anatomische Untersuchungen über die Beiträgen zur kortikalen Hemianopsie und Alexie*, Arch. f. Psychiat. **23**:609, 1891-1892; **24**:229, 1892). Shortly before death the patient recovered from mind blindness. This condition was reported in the examination

(Footnote continued on next page)

## ABSTRACTS OF CASES OF MIND BLINDNESS CONSIDERED GENUINE

GROUP I: *Cases of Mind Blindness Due to Compression of the Occipital Lobe.*

CASE 1 (Wendenburg<sup>45</sup>).—*Blow on the head; after a year attacks of loss of consciousness, forgetfulness, inability to recognize objects and astereognosis on the left. Parasagittal meningioma compressing the right cuneus.*

A man aged 41 suffered a blow on the head, after which he experienced fortification spectra. A year later there developed headache, forgetfulness and transient losses of consciousness. He paid little attention to his difficulties, which varied considerably. Then appeared "weakness of vision," and he became unable to recognize houses and to find his way about. He could not identify the things he saw. Sensation in the feet diminished; he lost his slippers and could not get them on. He also had a drawing pain in the neck and tinnitus in the right ear.

Examination on Feb. 20, 1904, revealed that he was slightly stuporous and hard to get along with but euphoric. He was unable to dress himself, putting his legs into the sleeves. When ordered to dress he took his clothes, turned them around and finally laid them down because he did not know what to do with them. He could not find the door to his room and had to be waited on like a child. There was left homonymous hemianopia. While there was no astereognosis, objects on the left felt larger than those on the right.

On November 18 he was still unable to dress himself, not knowing the arm-holes, but he distinguished the right from the wrong side of the coat. He talked well, telling stories of his military service, but was unable to find his way to the toilet. He also urinated on the floor without first trying to find the urinal. By Feb. 11, 1905, astereognosis had developed on the left. There was also complete atrophy of the optic nerve. The mind blindness lasted fifteen months.

Autopsy: As seen from the convexity, a mass, the size of a pigeon's egg, bulged forward in the right occipital lobe. At the right border of the sagittal fissure there was adherence to the dura. When this adhesion was removed the tumor fell out, having only compressed the brain substance, with which there was no connection. It proved to be the cuneus that had been compressed.

This case was one of a localized lesion affecting the right cuneus alone and not destroying the substance except by pressure from without.

on March 24, 1886. In the original article the author said: "Signs of mind blindness, apraxia and the like were never observed." However, the patient, who formerly had been a landscape painter, was afterward unable to draw. The designation mind blindness seems to have depended on this fact. (3) Case of Hun (Hun, H.: A Clinical Study of Cerebral Localization Illustrated by Seven Cases, Am. J. M. Sc. **93**:40 [Jan.] 1887). The patient had visual agnosia for objects for a short time on one day and subsequently after a tiring journey. Cerebral anemia might account for this. During the remainder of the time there was no visual agnosia for objects.

44. For lack of verification the case of Wohlwill (Wohlwill: Neurol. Centralbl. **34**:46, 1915) is rejected. The patient suffered a gunshot wound but recovered. One cannot be sure of the extent of the lesion in such a case.

45. Wendenburg, K.: Ein Tumor des rechten Hinterhauptlappens mit ungewöhnlichen klinischen Begleiterscheinungen, Monatschr. f. Psychiat. u. Neurol. **25**:428, 1909.

It was entirely unilateral in its effects. As the tumor was the size of a pigeon's egg, areas O, O<sub>1</sub>, O<sub>2</sub>, and O<sub>6</sub><sup>45a</sup> on the right may be considered as without function. The areas immediately below (O<sub>5</sub> and O<sub>3</sub>) were certainly affected. It is strange that there should have been astereognosis.

CASE 2 (Macewen<sup>46</sup>).—*Otitis media; cerebellar abscess on the left; subdural abscess covering the posterior portion of the temporal lobe and the occipital lobe and compressing these structures. Visual agnosia for objects; acoustic verbal agnosia. Drainage of the abscess; complete recovery from visual agnosia in four days and from acoustic verbal agnosia in another four days.*

In a man aged 52, suffering from mastoiditis secondary to otitis media, a cerebellar abscess developed on the left and was duly drained. At operation, there was observed, in addition, pus coming through the tentorium. Operation for this complication was delayed to see whether improvement would result from drainage of the cerebellar abscess. The patient's condition became worse; he became word deaf, answered irrelevantly and pursued his own course as though he had not been addressed.

From this point Macewen's own words are quoted, for the description is clear and observations only are given, without interpretation:

"The next day another symptom appeared. He seemed as though he did not see or could not understand what he saw. When he wished a drink, the vessel from which he usually received milk was placed right in front of him in line with his eyes, but he did not recognize it. All endeavors to attract his attention to it failed. Sometimes, however, he saw that an object was presented to him, and he would ask what it was. When his lips were touched with the spout of the drinking cup, he at once tried to drink, and his hands endeavored to catch the vessel. Again, if a vessel of another shape than that from which he usually drank was given him, it was evident he did not recognize by eyesight the altered form. . . . As soon as he grasped the vessel, he quickly recognized its form through the sense of touch. He could therefore understand neither what he heard nor saw."

"There was now sufficient evidence to warrant opening of the cerebral fossa, to expose the posterior aspect of the first temporal and the angular gyrus. This was done by removing a disc of bone over the first of these positions, when a wide cavity was exposed capable of containing over three ounces of fluid, and extending from the region of the first and second temporal convolutions at their posterior aspects backward and downward over the occipital lobe as far as the tentorium. . . . The cavity was in the subdural space and must have existed for at least months prior to opening. . . . The brain had been so much and for so long compressed that it showed no signs during the operation of regaining its former relation with the dura.

"The result of this operation was highly satisfactory. Within four days he regained the power of understanding what he saw, and this was followed four days later by clear indications of returning comprehension of spoken words. . . . His understanding was perfect, and he had no mental defect."

45a. O<sub>1</sub>, O<sub>2</sub>, etc., indicate numbered occipital convolutions.

46. Macewen, W.: Pyogenic Infective Diseases of the Brain and Spinal Cord: Meningitis, Abscess of Brain, Infective Sinus Thrombosis, Glasgow, J. Maclehose & Sons, 1893.

This case was clearly one of compression of the lateral surface, especially of the left occipital lobe. There was no appreciable destruction of tissue, as shown by the completeness of recovery. There is no doubt that the right occipital lobe was also compressed to some extent; however, this must have been from the mesial side, and the degree must have been small. Essentially, the lesion was unilateral (fig. 1).

**GROUP II: Cases of Mind Blindness Due to Superficial Softening of One Occipital Lobe.**

**CASE 3** (Luciani and Seppilli<sup>47</sup>).—*Visual agnosia for objects; jargon aphasia; acoustic verbal agnosia. Autopsy showed softening, confined to the cortex, affecting both temporal lobes but only the left occipital lobe.*

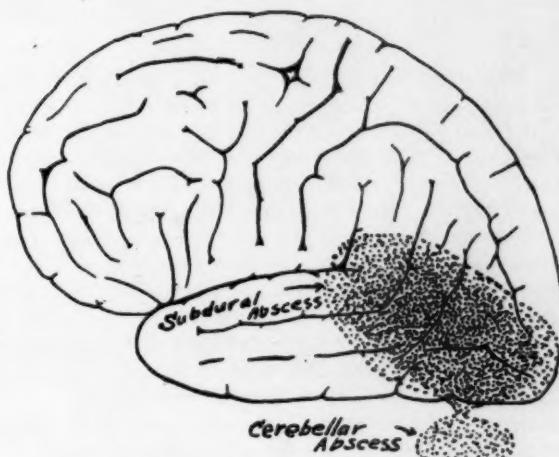


Fig. 1.—Diagrammatic representation of the lesion in MacEwen's case (case 2 in this series). The cerebral lesion was a subdural abscess, the brain being only compressed and recovery occurring soon after operative drainage. The lesion below was in the cerebellum, and this abscess had already been drained.

A woman aged 50, without a history to indicate the time of onset at the time of the first examination had all the symptoms enumerated and spoke with extreme jargon aphasia. She did not seem to understand the words addressed to her, although she showed that she heard them.

When brought into a brightly lighted room she looked about her, holding her head high and apparently paying no attention to her surroundings. She moved about carefully, holding her hands before her; as she approached objects, she avoided them easily. It was necessary to hand her food, for she did not recognize it. She did not react to a burning candle held before her.

A few days after the preceding observation she had another apoplectic insult, becoming paralyzed on the right side, and died seven days later.

47. Luciani, L., and Seppilli, G.: Die Functionslocalisation auf der Grosshirnrinde, German translation by M. O. Fränkel, Leipzig, Franz Deuticke, 1886.

**Autopsy:** In the left hemisphere a large, old yellow area of softening involved the first, second and third temporal convolutions and the supramarginal and angular gyri and included also the upper three occipital convolutions. The softening affected practically only the cortex, the white substance being involved only to the slightest extent. In the right hemisphere there were an old yellow area of softening affecting the upper portions of the three temporal convolutions and a small red, finely punctate area of softening, the size of a pea, in the knee of the internal capsule. The basal ganglia on both sides and the optic nerves and tracts were intact. (The record did not state the nature of the lesion in the final apoplectic insult, which caused death.)

The superficiality of the lesions is the striking pathologic observation in this case. Only the lesion in the left occipital lobe is germane to the subject discussed in this paper. The other lesions were extensive and caused severe aphasia but could not have been even partially the cause of the visual agnosia.

**CASE 4 (Poussepp<sup>48</sup>).**—*Visual aphasia, visual agnosia for objects and alexia. Focal area of softening affecting the posterior part of the angular gyrus and the superior occipital convolution on the left to a depth of only 0.125 cm.*

A married woman aged 22 was delivered of her first baby on Feb. 27, 1920. Thirty hours after delivery she began to suffer from headache and visual difficulties. She complained that she saw with only one eye (hemianopia?) and that everything was red. Soon after this she passed into coma and had generalized convulsions. The coma lasted eleven hours, and the temperature reached 39 C. (102.2 F.). For four or five hours after regaining consciousness she continued to see everything red, and the failure of vision in the one eye continued. She saw digits but could not count them. On the following day the eyegrounds showed only hyperemia; the extra-ocular muscles were normal. The fever decreased by lysis in one month.

Examination after nine weeks (May 6) gave the following findings: The patient saw and described objects at a great distance but was unable to name them. She could not tell whether a certain person was a man or a woman. On taking an object into her hand she was able to name it immediately. She spoke perfectly in three languages. She was unable to copy a rectangle drawn on the table, but when she traced one constructed with matches, she drew it without trouble. She was unable to draw a table when shown the picture, but if told to draw a table she did so. She wrote letters daily to her husband but could not read what she had written, nor could she read printed words. She read a few letters written for her. She was able to orient herself in the environment and took walks alone in the city. There was no hemianopia, but the visual fields were constricted.

She was examined again after a year, and the same condition was found. She had learned to read a little but soon forgot what she had acquired. In depression over her condition she committed suicide by taking morphine.

**Autopsy (fig. 2):** There were dilatation and stasis of the cerebral vessels and slight swelling of the cerebral tissue. In the posterior part of the left angular gyrus and in the left superior occipital convolution there was a focus of yellowish discoloration, which proved to be a detritiform softening of the cortex. Farther

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48. Poussepp, L.: Contribution aux recherches sur la localisation de l'aphasie visuelle, Presse méd. 31:564 (June 23) 1923.

down, below the superior occipital convolution (in the lower part of the second or in the third occipital convolution), there was an area about the size of a pea which was paler than normal. All this area was softened to the depth of 0.125 cm. Microscopic examination confirmed the softening and showed considerable destruction of nerve fibers in the white substance below the cavity. The vessels were thrombosed.

Poussepp commented as follows: "These lesions explain the clinical syndrome observed. . . . The alexia was referable to the angular gyrus, especially the posterior part. As for the visual aphasia I am inclined to ascribe it to the superior occipital convolution. This clinicopathologic observation appears to be of considerable interest in showing the relations between cortical and subcortical lesions of the left superior occipital convolution. Involvement of the white substance, especially of the occipital lobe, seems to explain the visual aphasia."

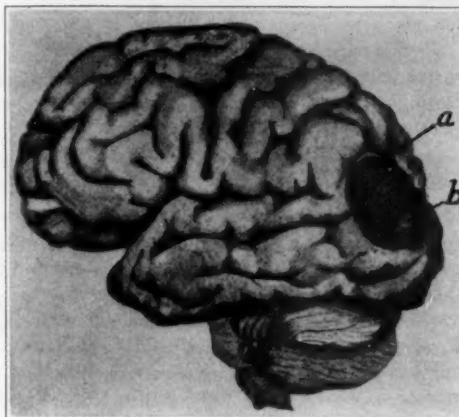


Fig. 2.—Poussepp's<sup>48</sup> illustration of the lesion in his case (case 4 in this series). The lesion affected the *pli courbe* (*gyrus angularis*) (a) and the superior (second) occipital convolution (b). There was also a small lesion in the third occipital convolution not shown in the illustration, which represents only the softening.

It is regrettable that the author did not show a section through the lesion stained for myelin sheaths. However, with a knowledge of the blood supply of the cortex, one can feel certain that the degeneration of the white matter was secondary to the cortical lesion. This case is, as nearly as possible, a crucial one, as there was no pressure, deep primary lesion of the white matter or other lesion, and death resulted from an extraneous cause.

It is true that the visual agnosia for objects was not complete; otherwise, the patient would not have been able to find her way about the city. There were also other elements in the case. It is probable that the lesion should have been a little larger, extending toward the mesial border and downward, to make visual agnosia for objects complete.

## GROUP III: Cases of Large, Deep Lesion of One Occipital Lobe.

CASE 5 (Henschen<sup>49</sup> [patient Abrams]).—*Agraphia; acalculia; visual agnosia for objects; visual hallucinations in the blind visual field; left homonymous hemianopia. Large area of softening in the right occipital lobe, extending deeply into the white substance.*

A man aged 60, who was right handed, was known to have acquired syphilis. He suffered a stroke of apoplexy, followed by forgetfulness, weakness and general carelessness. Examination showed left homonymous hemianopia, which caused the difficulty with reading usual in association with this lesion. Speech itself was undisturbed. He failed to recognize a bunch of keys and the fingers of the hand. He touched objects to identify them. As soon as he recognized them he could name them. He was able to read some words but made frequent mistakes owing to the visual defects. He was unable to write; even his name was poorly written. This syndrome lasted many months.

Autopsy: The left hemisphere was normal. In the right hemisphere there was a large area of softening in the occipital lobe, which had destroyed the lingual lobule and the greater part of the cuneus and extended deeply into the white substance. The posterior but not the lateral portion of the optic radiation was destroyed. The corpus callosum was degenerated.

This is a clearcut case of visual agnosia due to a lesion affecting only the right occipital lobe, in a man who believed he was right handed. In view of the aphasic manifestations, the right hemisphere must have been the major one.

CASE 6 (Lissauer<sup>50</sup>).—*Alexia, visual agnosia for objects; disorientation in space, from which the patient later recovered; optic aphasia for colors. Softening of the left occipital lobe, involving depth and convexity.*

A man aged 80, but well preserved, fell against a board partition, striking his head. He soon showed signs of hemianopia by running into objects. Then followed an episode in which he was unable to dress himself because he confused his garments, and he could not find his way about his home. He did not recognize his daughter. After this he improved and was well for a time.

Examination showed that he was disoriented for time and did not know addresses. On the other hand, there were no gross lesions of sensation or motility and no aphasia; there was complete right homonymous hemianopia. He was unable to select any color named but could divide specimens into groups without error. When fatigued he was unable to find his way around. Visualization of former images was good. He was able to write rapidly but could not read what he had written. He copied slavishly.

After six weeks he improved so that he was able to find his way about the city. He learned to recognize certain objects but failed regularly with others. When he failed to recognize by sight, he used touch and identified things well. He said that red liquid was "crystal clear" and clear water "black."

Autopsy (reported later by Hahn<sup>50</sup>): In the left hemisphere there was an old softening affecting accurately the cuneus. The lingual gyrus was also involved. The continuation of the splenium into the right side was degenerated. The follow-

49. Henschen,<sup>20</sup> vol. 1, p. 144; vol. 5, p. 31.

50. Hahn, E.: Pathologisch-anatomische Untersuchung des Lissauer'schen Falles von Seelenblindheit, Arb. a. d. Psychiat. klin. in Breslau, no. 2, 1895, p. 107.

ing summary of the fiber tracts involved was given by Hahn: (1) On the right the forceps was entirely degenerated; (2) on the left the stratum cunei proprium (H. Sachs), assuring communication with the opticomotor area, was degenerated; (3) the inferior longitudinal bundle, assuring connection with the sensory language area of the temporal lobe, was involved; (4) the stratum sagittatum internum (optic fasciculus) to the pulvinar was affected (the fasciculus which was conserved went to the convexity and did not serve for vision), and (5) the splenium permitting communication with the right hemisphere was degenerated.

It is clear that the visual fibers on the left side were destroyed, causing hemianopia, and that with the splenium destroyed visual impulses which may have come from the right hemisphere could not reach any secondary visual cortex on the convexity of the left occipital lobe. The patient had visual agnosia for objects in spite of the intact right occipital lobe.

**CASE 7** (Lountz;<sup>51</sup> abstracted by Nodet.<sup>19</sup>)—*Two apoplectic insults, followed by disturbance of vision and paresis; apparent blindness; visual agnosia for objects; disorientation; some tactile agnosia; softening of the internal two thirds of the right occipital lobe.*

A woman aged 55 suffered a sudden attack of vertigo with loss of consciousness in July 1895. This was of short duration but was followed by paresis of the left side and blindness. After this there was gradual amelioration of the condition. In January 1896 she suffered a new attack, with aggravation of the visual disturbance and difficulty in walking. The patient looked stupid; the eyes were fixed straight forward, like those of a blind person. Objective examination of the eyes gave normal results. The patient was less well oriented than a blind person and was unable to count fingers. The sense of taste was well preserved, and smell and hearing were less well retained. She mistook a crayon for the handle of an umbrella and a watch chain for the watch and applied it to her ear.

**Autopsy:** There was softening of the internal two thirds of the right occipital lobe, affecting the internal portion of the occipital horn. There was a second small focus at the tip of the occipital lobe. There were other small foci in the right lenticular nucleus, the thalamus and the caudate nucleus.

This case resembles the preceding one, except that the lesion was on the right side. In three of the cases so far described the lesion was on the right.

**CASE 8** (Hughlings Jackson<sup>6</sup>)—*Sudden appearance of visual agnosia for objects and disorientation; left homonymous hemianopia; visual verbal agnosia; fluctuating course; glioma filling the right temporo-occipital region.*

A woman aged 59 was apparently well until a day when she attempted to show a familiar park to a visiting relative. She became lost and was unable to find the gate to the park, although it was directly in front of her. She presented a different appearance from day to day, but the course was gradually downward. There developed alexia, although she was able to read letters to some extent. In the hospital she called all nurses "Annie," which was her daughter's name. She asked a nurse: "Are you the one that came just now?" She was unable to differentiate coins of various denominations. There was apparently left homonymous hemianopia.

51. Lountz, A.: Abst., Arch. de neurol., 1898, p. 85; cited by Nodet.<sup>19</sup>

**Autopsy:** A large glioma involved the entire right temporo-occipital region. It was largest in the temporal region, but a salient extended into the occipital lobe, terminating below the calcarine fissure. It destroyed the fibers of the splenium, as the tumor lay close to the mesial border. It was  $\frac{1}{2}$  inch (1.27 cm.) in diameter at its posterior portion (large enough to disorganize the occipital lobe).

This is the fourth case of this series in which the lesion was on the right side. There were aphasic manifestations as well, showing that the right hemisphere was the major one.

**CASE 9 (Rabus<sup>18</sup>).**—*Two apoplectic insults; visual agnosia for objects; ideokinetic apraxia; tactile agnosia on the right; large apoplectic cyst involving the left hemisphere from the frontal to the occipital lobe.*

A laborer aged 65 on Oct. 1, 1889, suffered an apoplectic stroke, followed by motor aphasia, from which he improved so much in the course of a year that he was discharged from the hospital. On Nov. 1, 1891, he suffered a second attack, after which he was unconscious for three days and improved gradually. When examination was possible, it was found that he paid little attention to his surroundings, not even accepting food until it was placed in his mouth.

As improvement continued, it became evident that he did not recognize objects about him. In the report (made in 1895) it is possible in only a few instances to differentiate between agnosia and apraxia, but a few citations are convincing. The patient failed to recognize a trumpet until it was blown, whereon he immediately blew it. (If the difficulty had been based on apraxia, he would not have been able to blow the trumpet even when he heard it.) It is clear from the account that he failed at times to recognize objects even when he handled them; i. e., there was also tactile agnosia in one hand. The patient did well in handling objects when he was shown. At times he exhibited apraxia also.

**Autopsy:** A large cyst involved much of the left hemisphere; it was irregular and superficial. There was a deep defect in the left second frontal convolution, which left intact hardly a centimeter of cerebral substance in the posterior portion. This was united with a similar defect, beginning in the posterior third of the third frontal convolution and extending to its posterior border. The region of the insula which was not covered by the outer surface of the brain was involved in the scar. The major portion of the superior temporal convolution was softened, and the second temporal convolution was affected to some extent in the anterior and middle portions. The third temporal convolution was intact. The postcentral convolution showed a defect, which extended to the border of the angular and supramarginal gyri. From that point a salient extended into the occipital lobe, reaching a point within 1 cm. of the occipital pole.

This case conforms to the general type in this group in that the calcarine cortex on both sides was separated from the convex surface of the left occipital lobe.

**CASE 10 (Müller<sup>52</sup>).**—*Gradual development of jacksonian seizures; visual agnosia for objects; visual aphasia for colors; right homonymous hemianopia; ability to read, with inability to recognize objects. Large tumor of the left occipital lobe.*

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52. Müller, F.: Ein Beitrag zur Kenntnis der Seelenblindheit (case 2), Arch. f. Psychiat. **24**:856, 1892.

A woman aged 56 in 1883 began to complain of headache and soon after also of attacks of visual disturbances, in which things went black before her eyes. After four years disturbances of sensation on the right side of the face appeared. In 1891 mental signs and mind blindness developed. Examination showed complete right homonymous hemianopia and constriction of the left field. Calculation and speech were good. For a time the patient was unable to name objects but recognized them. Then developed loss of recognition of objects. She recognized a pocket-knife, brush and pair of scissors only by touch, a bunch of keys by sound and a watch by its tick. She did not recognize a burning candle until burned by it, and she failed to identify pictures. She was able to recognize by taste but not by smell. She was unable to name colors but selected them on request. Revisualization of images was good; she named colors of things formerly known correctly. She was able to divide lines and geometric figures correctly and to draw from memory. However, she could not tell time. When not able to read by sight she read by tracing with her fingers. She could write from dictation.

Autopsy: There was a hard, bluish red tumor of the left occipital lobe, the size of a small apple. It was attached to the dura and reached into the tip of the lobe. It was not sharply separated from the gyri and was attached to the meninges by many small new blood vessels. The tumor compressed the right occipital lobe somewhat by extension across the midline. The adjacent softening reached forward and medially to the splenium of the corpus callosum and involved this structure. The cortex of the left occipital lobe was distinctly narrowed, as well as the cortex of the right on the mesial side.

It is probable that the slight compression of the right occipital lobe, especially on the mesial surface, could have had no detrimental influence on its function, except in a general way.

CASE 11 (Jack<sup>53</sup>).—*Visual agnosia for objects; visual aphasia; loss of power to revisualize former images; alexia (visual verbal agnosia); acopia; agraphia; amnesic aphasia; tactile agnosia in the right hand. Large tumor of the left temporal lobe and extensive softening of the left occipital lobe.*

In a man aged 63 the state just outlined developed gradually. "Such objects as matches, a key, comb, napkin, photographs, etc., brought up no remembrance of similar previous ocular images. Other objects he recognized but could not find words to express the name, or the idea vanished before he could put it into words." Jack distinguished between visual agnosia and visual aphasia. "For example, one day a key was held up; he could not tell what it was or its use and when put into his hands he was helpless; an attempt to draw it on paper was also a failure." There were failure to recognize by sight or touch [probably only in the right hand] and inability to draw. "When asked, he could not describe the school house across the way, nor the arrangement of the streets, and this was not due to lack of aural [ocular] perception apparently. . . . Former familiar streets were only partially or not at all recognized." The patient was also unable to read or to copy.

Autopsy: This revealed a tumor, 6 cm. in diameter, the posterior end of which was at the anterior border of the left occipital lobe, the upper margin at the level of the first temporal convolution and the inner border at the collateral fissure.

53. Jack, E. E.: A Case of Alexia, Mind-Blindness, etc., with Autopsy, Boston M. & S. J. **143**:577 (Dec. 6) 1900.

Below this was an area of softening involving the inferior surface of the temporal and part of the occipital lobe. In the left occipital lobe there was a mass, the central portion of which was soft and the outer reddish gray, extending upward to within 1 cm. of the upper margin of the first occipital convolution, downward and backward to the posterior border of the occipital lobe and inward to within 3 cm. of the mesial surface of the occipital lobe. So far as the occipital lobe was concerned, the destruction affected the subcortical region of the outer half, the cortex being spared but cut off from communication with the calcarine area of both sides.

This is a clear case of isolation of the left occipital cortex from the calcarine cortex of both sides. The clarity with which the author distinguished between visual aphasia and agnosia makes the case especially valuable.

CASE 12 (Giannuli<sup>54</sup>).—*Visual agnosia for objects; visual aphasia; disorientation in space; transcortical sensory aphasia; acoustic paragnosia; jargon aphasia; ideokinetic apraxia; tactile agnosia on the right. Cyst in the left occipital lobe, destroying the second and third occipital convolutions, and softening of the left temporal lobe.*

A man aged 77 had an episode characterized by a defect in visual recognition and disorientation within his own house. After this he suffered another stroke, which left him without power of spontaneous speech and little ability to understand what was said.

He stared before him like a blind person. He had right homonymous hemianopia and understood only the simplest commands such as "get up," "walk" and "sit down." He was able to repeat many words, though he did not understand what they meant. He did not recognize objects except in certain cases, and then he was unable to name them. When he was asked to select a watch from among certain objects before him, he was unable to find it until he heard it tick, when he immediately picked it up. (As he did not understand all that was said to him, one might suppose that he had not understood the request, but the fact that he picked up the watch when he heard the tick proves that he had comprehended and merely had not recognized the watch.) Giannuli related many instances of the patient's inability to select the proper object on request and to name objects by sight or even by touch, but these do not apply to the problem of visual agnosia for objects. The patient also had ideokinetic apraxia, as shown by his inability to handle objects placed in his hands; he was unable to cover himself, although he was cold and the covers were on the bed. He urinated into a dish or his hat, and when he was handed a glass of water or a spoon, he put the object into his pocket or let it fall.

Autopsy: There was extensive softening of the left temporal lobe, especially of the second and third convolutions. Most of the left occipital lobe was destroyed, including the lateral portions of the second and third convolutions. Ventrally there remained only a vestige of the lingual lobule. Mesially the convolutions of the cuneus were destroyed. All this portion of the occipital lobe was a cystic mass.

This case was difficult to study and report. In citing many of the acts in detail, the author did not differentiate between apraxia and

54. Giannuli, F.: Un caso di cecità psichica, Policlinico (sez. med.) **18**:194 and 273, 1911.

visual agnosia, and he assumed at times that the patient's failure to carry out commands was due to visual agnosia, when actually he probably had not understood the command. However, certain tests were unequivocal and established visual agnosia for objects.

**CASE 13 (Nodet<sup>19</sup>).**—*Visual agnosia for objects; some degree of tactile agnosia; visual aphasia for colors and possibly in general; agnostic alexia; slight paraphasia. Subcortical softening in the left occipital lobe and destruction of the splenium.*

A man aged 66 suffered a stroke which was not typical of ordinary hemiplegia. There was incomplete right hemianesthesia; the arteries were hard and tense; the pulse was full, and there was a slight cardiac murmur at the apex. In addition, it was necessary to feed the patient, for he did not recognize his food. It soon became clear that he either did not recognize objects about him or was unable to name them. A fork was a "rake," a bottle a "plant" and a key was "to put seeds into." His eyes were lively and followed things about, and he spoke with a slight paraphasia. A candle was a number, and when this was denied he did not know what it was. A nightcap was an "A" until it was placed on his head, when he



Fig. 3.—Tracings from Nodet's<sup>19</sup> illustrations of the lesions in his case (case 13 in this series). The left calcarine area was destroyed, as was the splenium. The lesion in the latter region prevented impulses from reaching the left occipital cortex from the right calcarine area.

recognized it. He identified anatomic parts of himself but not of others (use of the sense of touch). A cork was a "caterpillar" until he tasted it, when it was a cork. He knew a watch by sound but not by sight or touch. He did not recognize coins.

On the other hand, he was able to count fingers at 3 meters (yet counting is rarely possible in cases of visual agnosia). He could not name colors but classified them. He was able to judge distances and had stereoscopic vision. He also distinguished four or five geometric figures before him. He was able to read letters but not words. Everything looked gray to him.

**Autopsy (fig. 3):** The brain appeared normal except for the left occipital lobe, which was softened. After hardening in formaldehyde, there was observed softening of the internal portion of the left occipital lobe and a limited part of the left paracentral lobule. The cuneus in its entirety was softened to a point a few centimeters anterior to the parieto-occipital sulcus. Below, the softening extended to a point a few millimeters below the calcarine sulcus, which had disappeared. The

lingual gyrus was spared, except for the posterior portion, where the lesion extended to reach the fusiform gyrus, which was engulfed to the extent of about 5 cm. The collateral sulcus formed the limit at this level. Finally, posteriorly the lesion had distorted the point of the occipital lobe and extended to the convex surface 2 or 3 cm. over the third occipital convolution. Serial sections 5 mm. apart revealed the following: At the level of the cuneus the softening involved the gray substance in its entirety, penetrating deeply into the white matter and reaching the inferior and interior portions of the lateral ventricle. The inferior longitudinal fasciculus and the calcarine fissure had disappeared. The forceps major did not exist, and the splenium was destroyed on the left.

This case is valuable because of the unquestioned unilaterality of the lesion, the absence of pressure phenomena and the careful post-mortem examination.

#### ANALYSIS OF THE MATERIAL AND DEDUCTIONS

*Handedness and "Brainedness."*—In four of the thirteen cases described there were lesions on the right side. Two of the four patients presented aphasic manifestations, as well as visual agnosia for objects. This may reasonably be taken as evidence that the two patients were really left-handed persons who had in early childhood been converted to right handedness by their mentors. This explanation, however, does not apply to the other two patients, and, while a series of thirteen cases is far too small to be of statistical value, the occurrence of two additional cases in so small a series must, nevertheless, have consideration. The accepted proportion of left handedness in the population in general is about 10 per cent.

Are the major occipital lobe and the major temporal lobe in the same case not necessarily ipsilateral? Or does the natural handedness not necessarily correspond with the opposite brainedness? Perhaps "conversion by parents" does not explain "crossed aphasia" in all cases.

Recently, in consultation with Dr. Cyril B. Courville, I saw a right-handed patient who, after a severe injury to the head and unconsciousness lasting six and a half days, had still, two and a half years later, right homonymous visual agnosia for symbols and left homonymous visual agnosia for objects and colors. There is no escape from the interpretation that one occipital lobe was the major one for recognition of symbols and the other for recognition of objects.

Recently, with Dr. Samuel D. Ingham, I had the opportunity to see a case which shed light on another phase. A man aged 64, suffering from hypertension following an apoplectiform seizure, had right homonymous hemianopia, complete alexia for even what he himself had written and amnesic aphasia. These findings would not be unusual if it were not that he was and always had been left handed. He certainly

had not been converted from right handedness to left handedness by a well-meaning trainer. This was a case of so-called crossed aphasia in a left-brained, left-handed person.

With these facts in mind it is clear that one cannot determine which is the major occipital lobe by either the handedness or the brainedness.

*Localization of the Lesion.*—As shown by the opinions already abstracted, it is generally recognized that only the occipital lobes are concerned with recognition of objects by vision. I shall confine attention, then, to these areas. As all the thirteen cases reviewed in this paper represent instances of unilateral (occipital) lesion, it is concluded that a lesion in one lobe suffices to cause the syndrome. Within this lobe it may be possible to localize the minimal lesion to certain smaller areas.

In case 1 (Wendenburg) the lesion was confined to the cuneus, except for the indirect pressure on the convolutions below. In the accepted code, this means that areas O, O1, O2, and O6 were directly affected. The convolutions just below (O3 and part of O5) were compressed somewhat. One therefore should find the essential structure within this area. In case 3 (Luciani and Seppilli) and case 4 (Poussepp) the lesion was extremely superficial, in the latter only 0.125 cm. deep. In case 3 the entire occipital lobe was affected, but in case 4 only O2 and part of O3. In this instance, however, the loss of recognition was not complete, as evidenced by the statement that the patient took walks about the city alone after several weeks. It is necessary to admit that the lesion should probably have been somewhat larger to produce complete visual agnosia for objects. (I discount the significance of the lesion in the angular gyrus and ascribe to this structure the recognition of written words, which is well established.) That there was secondary degeneration below this cortical lesion does not apply, for agnosia was present immediately after the vascular lesion occurred.

The cases in group III should furnish data concerning the portion of the deep structures involved. In case 5 (Henschen), case 6 (Lissauer), case 9 (Rabus), case 10 (Müller) and case 12 (Giannuli) practically the entire white substance of the occipital lobe was destroyed. In case 7 (Lountz), case 8 (Jackson) and case 13 (Nodet) the lesion was confined to the mesial portion. In case 11 (Jack) the lesion was confined to the lateral portion. In every case in group III there was destruction of the corpus callosum or its continuation in the forceps major. With this information and the illustration (fig. 4) as reference, it is clear that with the splenium involved no impulses could reach the major occipital cortex from the opposite calcarine cortex. The problem

then reduces itself to a consideration of the transverse fibers shown on the left, passing from *K* (calcarine area) to *O<sub>2</sub>*. These fibers are the transverse occipital fasciculi of Sachs and Vialet. As one is dealing with a fiber system, it is not strange that destruction of either end should give the same result. This scheme, then, which harmonizes with the ideas of Wilbrand and Sänger, Henschen, Bonvicini<sup>55</sup> and others, seems essentially correct. (The entire scheme is reversed for right-

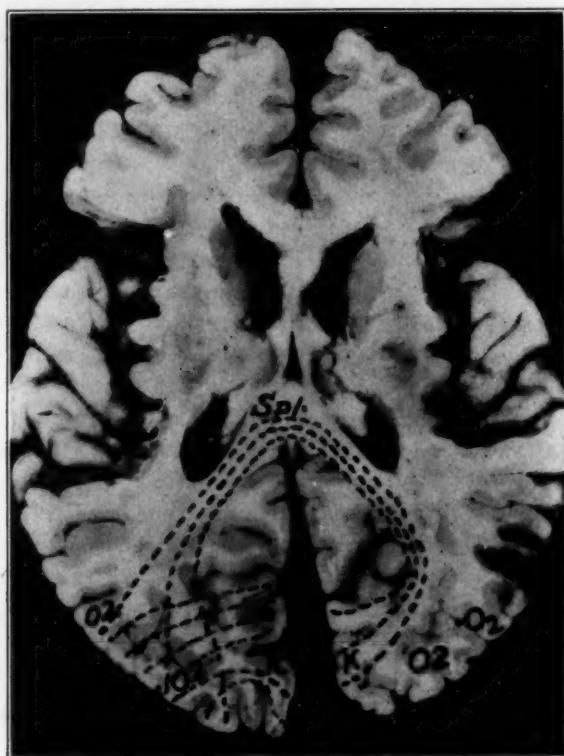


Fig. 4.—Diagram superimposed on a photograph of a dissected specimen, showing the simplest possible pathways from the calcarine areas of the two sides to the cortex of the left second occipital convolution. The diagram represents not all, but merely two essential, pathways traveled by impulses in the recognition of objects. The actual pathways are infinitely more complicated.

55. Bonvicini, G.: Die Störungen der Lautsprache bei Temporallappenläsionen. Die Entwicklung der Lehre der Temporallappenaphasie, Theorien und Erfahrungen, in Alexander, G., Marburg, O.: Handbuch der Neurologie des Ohres, Berlin, Urban & Schwarzenberg, 1929, vol. 2, pt. 2, pp. 1570-1868.

brained persons.) All cases in the literature which have been abstracted harmonize with this concept. Figure 5 shows the cortical area seemingly essential for the recognition of objects.

In all fairness, however, it should be stated that not all authors have accepted this idea. Von Monakow<sup>9</sup> expressed disagreement in the following statement:

The localization outlined has been suggested by several authors (Wilbrand, Nothnagel, Flechsig, Henschen and others), namely, two functionally separate regions in the occipital cortex, one especially for optic awareness and another for optic memories. The region for awareness was placed in the mesial cortex and the region for memory in the remaining portion of the occipital cortex. Such a concept is, indeed, convenient but is too much in opposition to the views of general physiology and the pathologico-anatomic observations available to date. Besides,

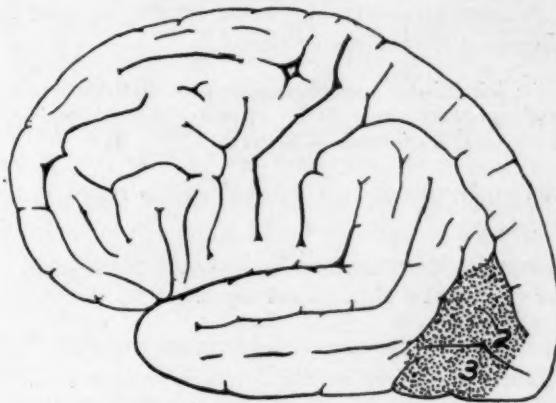


Fig. 5.—Areas of the cortex (on one side or the other) considered essential for the recognition of objects. The area shown here is not the "location of the visual images" of objects, a great portion of the cortex being necessary for this function, but merely the essential area; a lesion here suffices for loss of the function. The left side is not necessarily the major side in every case.

it is physiologically too crudely elaborated to be satisfying. At any rate, the concept is not capable, to even a reasonable degree, of clarifying on an anatomic basis the complex processes which are under consideration.

The question of "negative cases" should also have consideration. Henschen<sup>20</sup> listed a considerable number of so-called negative cases. They were selected, however, as instances of mind blindness and not strictly of visual agnosia for objects. According to the criteria followed in the selection of cases in this work, the cases of Weissenberg and Henschen are actually true, or "positive" instances. When carefully reviewed, the others are found not to be negative. If the anatomico-physiologic concept presented in this paper is correct, one can readily

see how a patient may have a lesion of the left occipital lobe or even of both occipital lobes and still not have visual agnosia for objects. There are certain definite structures which must be affected before the syndrome results.

The concept presented in this paper and shown diagrammatically in figure 4 may be subjected to test in another way. With reference to the diagram, one can readily see what the result would be if the splenium of the corpus callosum alone were severed. If the patient was left brained he should have visual agnosia for objects in the left half of the visual field. A review of the literature failed to reveal any case of this sort. Probably this is due to lack of tests for the condition, as the defect certainly would not be found unless specifically sought. However, there is support from another source. Hartmann,<sup>56</sup> in his excellent monograph, presented reports of several interesting cases. In case 4 in his series (page 124) the report stated:

Tumor of the left inferior parietal region, with disturbances of fixation and localization in the opposite visual field, and severe disturbance in the estimation of distance; no general disturbance of orientation.

There was no hemianopia. In case 5 in his series (page 127) the report stated:

Focus of softening in the left parieto-occipital region? Disturbances of attention and interest for events in the right field of vision.

The patient seemed not to see objects in the right field but was found to see them when her attention was called to them. The defects in these cases might easily have been called mind blindness by another author. Certainly, Hartmann had the idea which I have suggested—that disturbances may occur in one half of the visual field. Recently Riddoch<sup>57</sup> reported visual disorientation in homonymous half-fields, and Drs. Ingham and Von Hagen studied a similar case at the Los Angeles County Hospital.

It occurred to me that as operation for removal of a pineal tumor requires severance of the splenium of the corpus callosum, it might be possible to examine a patient before such an operation and again immediately afterward on the operating table, when the operation is performed with the use of local anesthesia, before damage is done to the neighboring structures in the completion of the operation. This should be done at the earliest opportunity.

56. Hartmann, F.: *Die Orientierung*, Leipzig, F. C. W. Vogel, 1902.

57. Riddoch, G.: Visual Disorientation as the Sole Defect in Homonymous Half-Fields: Two Cases, *Brain* **59**:376, 1935.

## SUMMARY AND CONCLUSIONS

The weight of the evidence presented in this paper is strongly in favor of the following:

1. One occipital lobe is dominant over the other for recognition of objects.
2. The dominant lobe is usually the left but may be the right, even in right-handed persons.
3. Within the occipital lobe the cortex of the second and third convolutions represents an area which is essential for the recognition of objects. It is not correct to say that here lie memory pictures, for a large part of the brain is utilized in constructing them, but visual memory pictures cannot be evoked without the function of this area.
4. Impulses reach this area via the transverse occipital fasciculi of Sachs and Vialet from the same side and via the splenium of the corpus callosum from the opposite side.
5. The so-called negative cases cannot be considered as such merely because the left occipital lobe was destroyed.
6. Cases of lesions in both occipital lobes do not necessarily disprove the concept presented here. In order to disprove it, the specific fiber tracts or cortical area of the major occipital lobe must have been destroyed without producing visual agnosia for objects.

NOTE.—As stated before, it would be desirable to have studies of a case in which the splenium of the corpus callosum was severed for removal of a tumor from the third ventricle. If the concept outlined in my article is correct, the patient after such an operation should have visual agnosia for objects in the left field of vision.

Just as the galley proof of my article had been returned to the publisher, I received the April number of the *ARCHIVES OF NEUROLOGY AND PSYCHIATRY*, in which Dr. John H. Trescher and Dr. Frank R. Ford reported such an operation performed by Dr. Walter Dandy and subsequent studies. They found visual agnosia in the left field of vision. They said: "She would be conscious of something to her left but would not recognize it."

## ABSTRACT OF DISCUSSION

DR. A. L. SKOOG, Kansas City, Mo.: I worked on this subject years ago and at that time was struck with the difficulty especially in finding a case of pure mind blindness. Since Dr. Nielsen asked me only in the last two weeks to substitute in the discussion, I have recently reviewed the literature and find that Dr. Nielsen is correct in stating that there are few cases of unilateral lesion in which visual agnosia was demonstrated.

One might criticize Dr. Nielsen for being so critical as to what cases he should admit when he draws hard and fast conclusions regarding the unilateral dominance or the localization of visual agnosia in the occipital cortical region.

He has called attention to the possible value to be derived from studies of association pathways, especially those from left to right or right to left in the occipital region.

I agree with Dr. Nielsen regarding the localization of visual recognition in the second and third convolutions of the occipital lobe. How much preponderance of domination exists on one side or the other, depending on whether the individual is left handed or right handed, is still a problem. Because of this I suggest the great importance of clinical studies relative to visual agnosia and carefully conducted autopsies, when possible.

I cannot conceive that experimentation on animals will help in the study of this problem, for one cannot utilize written or verbal speech in the animal as one can in the human subject. Therefore, it becomes necessary to rely on autopsy for more accurate deductions. It is along this line that after careful study of a number of cases reported in the literature, dating back one hundred years, Dr. Nielsen has made his deductions and standardized the cases that should be accepted.

Dr. Nielsen has suggested several varieties of agnosia—visual, auditory, tactile, olfactory and gustatory. Probably the visual and tactile types are more readily discerned than the other three.

DR. WILLIAM L. NELSON, St. Louis: I have never been satisfied with the concept of cerebral dominance, although I am a person who believes a great deal in "hunches" and who acts on them often.

I hoped from the presentations yesterday of the action potential of the brain that one might get a "lead" in regard to this question of dominance of the brain, but I saw nothing that would give me much on which to proceed.

There are persons who are right handed and left eyed and perhaps left legged, and vice versa. There may be combinations of responses on the part of the subject that indicate a certain lack of harmony in the dominance of the two sides of the brain. Then, again, one finds persons who are left handed in one thing and right handed in another. There are persons who use both sides of the body at the same time. The question comes up as to what dominates the two sides. One sees persons who have had training that enables them to engage simultaneously in one action with one hand and in a different action with the other. One wonders where the dominance lies and what is responsible for it.

I believe that there are functional representations in the cerebral cortex. I am not at all sure that they occur singly or unilaterally. I should be interested if Dr. Nielsen would comment on the question as to what experience the patient had after the deletion of function as a result of a gross lesion in this area of the occipital lobe.

He spoke of a woman who lived about thirteen months after an operation on this region, but he made no mention as to her training experience afterward.

I have a number of beliefs, which include an idea based on the training experience of subjects that determines the use of the brain, whether it is synchronous on the two sides or separate. I do not believe that Dr. Nielsen's demonstration proves that there is not some way of establishing a compensatory function.

Some of the members, no doubt, have read of what Shepherd Ivory Franz did in cases of homilateral disturbance. I saw some of his patients, as well as a number of motion pictures showing restoration of function. The question arises as to whether there are accessory or supplemental structures involved on the

opposite or the same side of the brain and whether these may not come into function.

DR. HANS H. F. REESE, Madison, Wis.: Do you propose to replace the rather general term asymbolia by a specific descriptive word, such as visual agnosia? I agree that in your work it would be better to call the syndrome of asymbolia visual agnosia, for it directs attention immediately to the anatomic lesion under discussion.

DR. J. M. NIELSEN, Los Angeles: Asymbolia was the term in common use prior to its replacement in 1891 by Freud's term agnosia. However, asymbolia was both sensory and motor, and it was only "sensory asymbolia" which was replaced by the term "agnosia." Asymbolia is a much broader term, and agnosia is highly specific.

Regarding restoration of function, I can say only that this is indeed slight when the lesion is so situated as to produce agnosia. The idea that restoration is common is based on the fact that transient agnosias result from lesions which occur in the neighborhood of the specific areas so that the symptom is dependent only on edema. All cases of this type were excluded from the report as it was given.

## CONTRIBUTION TO THE HISTORY OF NARCOLEPSY

HARRY A. CAVE, M.D.

LONDON, CANADA

To the historically inclined as well as to those interested in narcolepsy and allied conditions, the following report of a case will prove interesting and enlightening.

In a previous communication<sup>1</sup> on narcolepsy, I made the statements that narcolepsy was first described in 1877 by Westphal and that up to the present there had been no published report of autopsy in a case of narcolepsy. Both these statements now stand in need of revision, as shown by the following report of a case published by Dr. Richard Bright,<sup>2</sup> in January 1836, which I recently found. To Bright, therefore, belongs the credit of being the first to describe clinically and to perform an autopsy in what appears to be a typical case of narcolepsy.

The following history of a case, which is reported verbatim, is the fifth in a series of eleven cases of diseased arteries of the brain.

### CASE 5.—*Lethargic Symptoms and Apoplexy, with Disease of the Internal Carotid Arteries.*

Mrs. W., aged 67, has been, for the last thirty or forty years, subject to a most remarkable drowsiness, for which, even at the beginning of that period, she consulted a great many medical men, but never obtained any permanent relief. It is now fully ten years since she first spoke to me of her complaints; telling me that at all hours of the day she was liable, whenever she sat down, to fall into a profound sleep, and this happened sometimes even whilst she was eating her dinner. I gave her a variety of laxatives and gentle tonics, and recommended issues, and occasional local abstraction of blood in small quantities, by means of cupping; and for a time she improved a little; but these, like all other means, lost their effect; and latterly she has even been worse. Her daughters tell me, that not only has she been unable for years to follow any sedentary employment, but that if she attempted to work, read, or write, she infallibly fell into a sound sleep; and even when she sat down for a short time, she was apt to have what she called 'a shaking fit,' in which her hands would begin to be agitated, her head would fall as if the muscles of the neck had lost all power, and her features would become distorted.

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From the Department of Medicine, the University of Western Ontario Medical School.

1. Cave, H. A.: Narcolepsy, Arch. Neurol. & Psychiat. **26**:50-101 (July) 1931.
2. Bright, Richard: Cases Illustrative of the Effects Produced When the Arteries of the Brain Are Diseased, Guy's Hosp. Rep. **1**:9-40 (Jan.) 1836.

Under these attacks, the only thing they found of the least service was raising her from her chair, and dragging her about the room; by which means she used to be gradually brought to herself. As far, however, as she had the power, she would always try to oppose this compulsory exertion, which was very irksome to her; and would only move about her legs, which seemed sometimes to have the desired effect. She often complained, latterly, of a darkness and obscurity of vision, chiefly on one side; but I do not remember, nor do her daughters, who never left her, that she ever spoke much of headache, either external or internal.

I had not seen her for many months, when I was one day suddenly called to visit her, about twelve o'clock; and learned she had been for some days labouring under a catarrhal affection, to which had been ascribed an increase of the usual lethargic symptoms, that had been observed during that time. She had risen, as usual, that morning about eight o'clock, and was heard to cry out, as if for help, before she reached the bottom of the stairs. Her daughters came immediately to her assistance, and found her unable to articulate intelligibly, and completely powerless on the right side. Mr. Dunn saw her within a very short time from the attack, and bled her, but without relief; and when I saw her at mid-day, she was lying in a state of apparent unconsciousness, and perfectly hemiplegic on the right side. Her eyes were half open, and she was throwing from her stomach a quantity of green, bilious, acid fluid: pulse 110, weak, and sometimes intermitting. She occasionally raised the left hand, as if catching at some object in the air. Blisters were applied and purgatives and injections were administered. She continued to vomit frequently, never recovered the least consciousness, and died at seven o'clock the following morning.

SECTIO CADAVERIS, hor, xxvij post mortem.—When the calvaria was removed, the vessels of the dura mater appeared numerous, and inclined to bleed. The longitudinal sinus was rather large, and quite empty. In raising the dura mater, no unusual adhesion was observed; but a tumor, of the size of a filbert, and of a hard and chronic character, grew from the under surface of that membrane, and had made a well-defined depression of a corresponding size, about the centre of the right hemisphere, near the vertex; but had contracted no adhesion to the arachnoid. It was at once obvious that the convolutions of the left hemisphere were flattened. There was no serum under the arachnoid, nor was the membrane opaque; and it was easily detached from the brain. The outer layer of the cineritious substance did not peel off more easily than it does in a healthy subject. Under the arachnoid, just above the ear, on the side of the middle lobe of the left hemisphere, blood was effused, but in a small quantity, looking like an extensive ecchymosis. Upon slicing off the hemispheres, the medullary matter appeared rather more dusky, and marked with more bloody points than is quite natural; and, on examining further, it was found that a large effusion of blood had taken place into the substance of the optic thalamus and posterior part of the corpus striatum on the left side, and had torn its way into the left ventricle; and a large and solid clot was found filling and distending all the posterior part of that cavity. The septum lucidum was so much softened and lacerated, as to be discoverable only by its fragments. The posterior part of the right ventricle was full of fluid blood, but contained no coagulum; a clot of blood was also lodged in the fourth ventricle. The choroid plexus, on each side, was rather granulated, and had a few vesicles in its structure.

Examining the base of the brain very carefully, we found the vessels much diseased; and this was much more the case in the carotids, and the vessels connected with them, than in the vertebrals and their branches; and more on the left than on the right side. Indeed, the vertebral arteries within the cavity of the skull had no obvious disease, except a little firmness, without discoloration, in that of the right

side, and the basilar artery was only slightly mottled with a white deposit; but the internal carotids, just where they enter the skull, were ossified, so that on the left a perfect bony shell was found, such as we very seldom discover. All the vessels ramifying through the fossa Sylvii, on that side, were spotted with yellow matter, and were much contorted and corrugated in appearance. In the right fossa Sylvii the vessels were also diseased, but in less degree. None of the vessels which reached the surfaces of the hemisphere had any obvious deposit in their coats. The sinuses of the base of the skull were by no means uncommonly large. The cerebellum, pons Varolii, and medulla oblongata presented no morbid appearances; except the clot of blood which has already been mentioned, as having escaped from the lateral ventricles.

In this case, it cannot be doubted that the disease found after death would enable us to account rationally for those lethargic symptoms by which the patient was oppressed during so many years: but how far there was sufficient peculiarity in the distribution of the vascular disease, to account for one symptom being so prominent above the rest, can only be inferred from extensive and accurate observations in a very difficult and complicated department of pathological investigation. Looking at the matter as one of reasoning and induction, rather than of observation and fact, we should certainly be inclined to expect that the suspension of the waking faculties would be chiefly brought about by disease in those two vessels which perform so principal a part in the distribution of blood to the hemispheres of the cerebrum; and consequently, when a state of lethargy is connected with such other symptoms as would induce us to infer disease of the vessels, we should chiefly direct our suspicions to the carotids, as the source of that affection.

There is, in this case, another point of some interest; I mean the peculiar 'shaking fits' to which this patient is stated to have been subject, and which formed a remarkable peculiarity in the course of symptoms. Now, it appears probable, that this peculiarity was in some degree accounted for by the tumor growing from the dura mater; which was very capable, as I conceive, of producing that species of irritation which so often manifests itself by epileptic and convulsive affections, when the surface and membranes of the brain are diseased.

The preceding description is so clear that there can be little doubt that Bright was dealing with the symptom complex that today is recognized as narcolepsy. The drowsiness and sleeping attacks, extending over a period of thirty or forty years, as well as the occurrence of the "shaking fits" or cataplexy, in which the patient's hands would begin to be agitated, her head would fall as if the muscles of the neck had lost all power and her features would become distorted," are of sufficient clarity to make the diagnosis possible at once. Bright did not, however, recognize the two symptoms as being the component parts of one clinical entity. He ascribed the shaking fit to the irritation produced by the tumor growing from the dura mater, an idea which many years later found a champion in J. Hughlings Jackson (1835-1911). Bright's knowledge and conception of the mechanism of epilepsy were quite modern, as shown by his remark in the same article "we know that irritation upon the surface of the brain from disease or accident will apparently become the cause of epilepsy."

The causative factor in the sleeping attacks he attributed to disease of the internal carotid vessels rather than to a disease of the brain substance itself, although he probably implied the latter. After citing several cases of pain in the head associated with disease of the carotid and vertebral arteries, he said :

I shall now venture one step farther into the path of a somewhat conjectural diagnosis by stating that in those cases where disease of the vessels is attended with unusual symptoms of lethargy, and the superficial pain of the occiput is less observable, it is, in my opinion, probable that the disease has been situated chiefly in the internal carotids and their branches.

In further support of the same idea he described another case under the title "Extensive Softening of the Brain with Very Advanced Disease of the Arteries." After reporting the history and describing extensive atheromatous changes in the carotid and basilar arteries, he said :

Since this case was sent to the press I have learned, for the first time, that the subject of it was, during the last twelve years of his life, affected with lethargic somnolency, to such an extent that he could scarcely keep awake, even when occupied in business or at table; and this fact, taken in connection with the state of the carotids tends to render the correctness of the diagnostic indication insisted upon in Case 5 still more probable.

While the memory of Dr. Richard Bright (1769-1858) has come down to posterity through the medium of his work on disease of the kidneys, it is to be noted that he was also interested in attempting to elucidate the complexities of the nervous system purely from clinical observation and gross pathologic changes. He made numerous original observations and contributions in this field, many of which have been overshadowed or virtually lost to the medical world by the halo cast about him by his work on albuminuria and renal conditions. By any one interested in the early development of knowledge of the nervous system, the works of Richard Bright should not be overlooked.

## Obituary

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MICHEL von LENHOSSÉK  
1863-1937

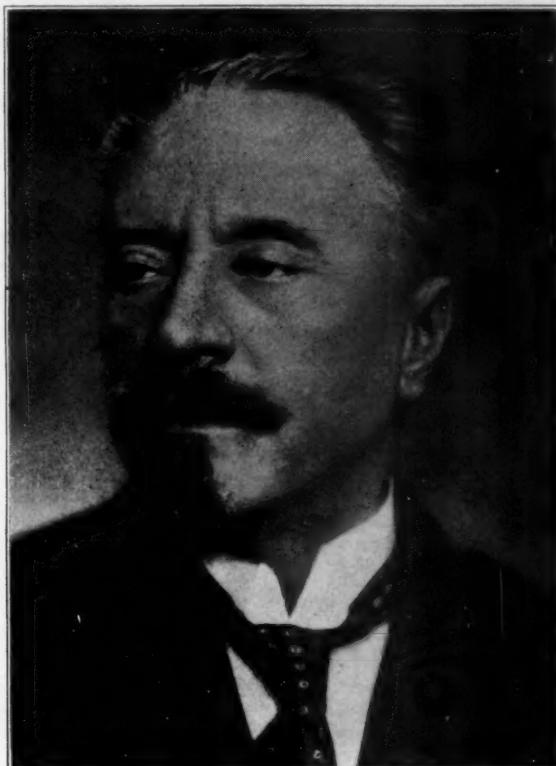
On Jan. 26, 1937, died Michel von Lenhossék, professor emeritus of anatomy in the University of Budapest and vice president of the Hungarian Academy of Sciences. Thus passed away the last of the great personalities of the heroic age of neurohistology, in which the neuron theory was developed and established.

Lenhossék's ancestors were craftsmen in Pressburg, the town in which the Hungarian government resided during the century and a half of Turkish occupation of the capital. The family was introduced into academic and scientific life by the grandfather, also named Michel. In 1809 he became professor of anatomy and physiology in the University of Budapest and in 1819 professor of physiology in the University of Vienna, but he left this position to become the head of the public health department of the Hungarian government and president of the medical faculty of the University of Budapest. His son, Joseph, became an anatomist and taught the subject at the University of Budapest. In that town Michel Lenhossék was born, on Aug. 28, 1863. When he obtained his medical education, the environment was proper to awake his interest in neurohistologic research. His father was the author of one of the earliest monographs on the structure of the spinal cord and bulb. The head of the second anatomic institute, Professor Mihálkovics, was also interested in the nervous system and was the author of a work on the development of the brain which is still classic. Under the influence of such teachers and impressed by the new discoveries in the field of theoretical neurology, Lenhossék made his début in medical literature with contributions to comparative neurology based on investigations by different morphologic methods. But it was the Golgi method which found in him one of its principal exponents.

After his father's death, in 1889, Lenhossék left Budapest and became prosector of the anatomic institute in Basel, Switzerland, then directed by the renowned embryologist Kollmann. Here he became professor extraordinary in 1891; in 1893 he moved to Germany, first to Würzburg, with Kölliker, and then to Tübingen, with Froriep. After the death of Mihálkovics, in 1900, he was appointed head of the first anatomic institute in Budapest, which he directed until his retirement, in 1933.

Many results of the scientific work of Lenhossék are now fundamental parts of knowledge. Such generally used terms as astroblast,

astrocyte and tigroid substance were first proposed by him. In one of his first papers he supported the pseudo-unipolar character of spinal ganglion cells and described the differences which distinguish the central from the peripheral process. Today this characteristic of spinal ganglion cells is accepted without question, but a perusal of the controversies of the early eighties will show the difficulty with which it was established.



MICHEL von LENHOSSÉK  
1863-1937

It is not possible here to give a detailed survey of Lenhossek's contributions to the development of neurohistology. One may mention, however, his monograph "Der feinere Bau des Nervensystems." Some of his researches were of clinical importance. When, in 1889, he described, at about the same time as Ramón y Cajal, the existence of centrifugal fibers in the posterior spinal roots, this seemed only a simple anatomic fact; but Lenhossek soon showed the relationship of this observation to the regulatory influence of the posterior roots on vaso-motor dilatation, as demonstrated by Stricker and others.

Besides his duties as teacher and his investigations in various fields of anatomy, Lenhossék returned to neurologic problems also in his later years. In 1905 he published a paper on the histogenesis of peripheral nerves, but his work in this field was overshadowed by the experimental studies of Harrison. Later his attention was given to the cytologic structure of the autonomic cranial ganglia.

Lenhossék's original contributions to science, important though they were, do not exhaust his significance to medicine. Citizen of a small country, writing and lecturing for his own countrymen, his influence naturally was exerted primarily at home. Yet he won recognition throughout the scientific world. He belonged to the type of scientist, now increasingly rare, who is able to combine the ability to do effective research in some restricted field with a wide mastery of the whole biologic discipline. He had an amazing knowledge of the entire biologic literature, and his morphologic researches were guided by this broad biologic orientation—hence his great influence on his pupils, in no matter what field of biology or medicine. They will keep alive the memory of his personality, as science will remember his original investigations.

STEPHEN KÖRNYEY, University of Szeged, Hungary.

## Abstracts from Current Literature

### Physiology and Biochemistry

DIFFERENTIAL OXYGEN UPTAKE OF REGIONS OF LIMULUS OPTIC NERVE AS RELATED TO DISTANCE FROM THE SENSE ORGAN. RITA GUTTMAN, Biol. Bull. **69**:356 (Dec.) 1935.

The differential rate of oxygen uptake of the optic nerve of Limulus polyphemus was investigated by means of a differential volumometer. Thirteen experiments are reported. In every case the respiration of the distal end was lower than that of the proximal region. The respiration of the distal end was lower than that of any other region of the nerve in all but one experiment. A maximal rate was found along the central portion of the nerve in ten of twelve cases.

COBB, Boston.

CHEMICAL STUDIES ON THE ADRENAL CORTEX: I. FRACTIONATION STUDIES ON HORMONE CONCENTRATES. J. J. PFIFFNER, OSKAR WINTERSTEINER and HARRY M. VARS, J. Biol. Chem. **111**:585, 1935.

Pfiffner, Wintersteiner and Vars report on the progress they have made toward purification of the hormone of the adrenal cortex. Fractions were assayed for their potency by determining the minimum daily dose which, when administered over a period of seven days to adrenalectomized dogs, maintains the blood urea nitrogen and the clinical condition of the animal at an essentially normal level. Most of the chemical and physical data indicate that the hormone is lipoid and water soluble, is not a nitrogenous compound and contains practically no sulfur or ash. In the cold it forms a hydrazone with phenylhydrazine with great ease. Ultraviolet absorption spectra indicate the presence of an alpha-beta unsaturated ketone in the active fraction. The authors were unable to crystallize the hormone.

PAGE, New York.

THE ELECTRICAL EXCITABILITY OF THE MOTONEURONES. R. LORENTE DE NÓ, J. Cell. & Comp. Physiol. **7**:47 (Oct.) 1935.

The soma of the motoneurons (body and dendrites with synaptic surfaces) is electrically excitable and has a lower threshold than the axon; furthermore, in so far as the response to electrical stimuli is concerned, both have the same elementary properties. The electrical threshold of the soma is lowered while the spikes of action potentials of nerve impulses are arriving at the synapses. However, the effect of nerve impulses and those of electrical shocks are not entirely identical, because the former set up responses of the motoneurons after a synaptic delay of about 0.7 sigma, while the latter set up responses without measurable latency.

The conditions for summation of nerve impulses arriving at different synapses on a motoneuron are discussed on the basis of the experimental evidence. It is concluded that for effective summation the following conditions must be fulfilled: (a) The impulses must arrive simultaneously, i. e., with an interval no longer than 0.25 sigma, and (b) the activated synapses must be in immediate proximity.

CHORNYAK, Boston.

A PHYSIOLOGICAL STUDY OF THE CEREBRAL MOTOR CORTEX AND THE CONTROL OF POSTURE IN THE SLOTH. ORTHELLO R. LANGWORTHY, J. Comp. Neurol. **62**:333 (Oct.) 1935.

The sloth is a tropical animal which normally hangs from the limbs of trees. Three animals of each of two species, the tridactyl and the didactyl, were studied.

With the animal under ether anesthesia, the cerebral cortex was explored with a stigmatic electrode mounted on a delicate string. The response was observed always on the side opposite to that of the stimulated cortex. All responses were slow and deliberate, corresponding with the rate of activity in the normal animal. The two-toed animals responded somewhat more quickly than the three-toed. The responses of the facial musculature were better differentiated in the didactyl species. The snout also showed greater differentiation in this type. The hindleg had much less cortical representation than the foreleg, and the movements of the hindleg were generally associated with contractions of the axial musculature. In the sloth the flexor muscles are antigravity muscles. The extensor muscles were most prominently represented in the cerebral cortex, as would be expected, since these muscles are used for reaching out for food and support. External and internal rotation of the legs was also marked. Stimulation of one area caused the body to be curved to the opposite side, through the contraction of the panniculus carnosus.

ADDISON, Philadelphia.

THE EFFECT OF LESIONS IN THE CENTRAL NERVOUS SYSTEM OF THE RAT UPON  
REFLEX TIME. R. YORKE HERREN, LEE EDWARD TRAVIS and DONALD B.  
LINDSLEY, *J. Comp. Neurol.* **63**:241 (Feb.) 1936.

The effects on the reflex time of lesions variously placed in the cerebrum, the cerebellum, the corpus callosum, the caudate nucleus and the spinal cord in the rat are presented in this paper. The latencies of the reflexes were determined by the action current technic. Records were taken of the reflex of the achilles tendon and of the crossed dorsiflexion of the foot in all animals. To determine the extent of cortical damage, the brains were removed and sectioned serially and every tenth section was examined microscopically. The mean achilles reflex time of all rats before operation was 6.8 milliseconds, with a range of from 6.3 to 7.5 milliseconds. The mean crossed flexion reflex time of all rats before operation was 10.3 milliseconds, with a range of from 9.2 to 11.5 milliseconds. In no instance, regardless of the locus or the extent of the lesions, was there any significant change in the reflex time for crossed flexion after operation.

Lesions in the cerebral hemisphere produced decrease in the latency of the achilles reflex on the side contralateral to the site of the lesion. The extent of the lesion was not related to the degree of reduction in the reflex time. Within three months the latency of the reflex time on the side of the lesion returned to the normal, as represented by that on the normal side. Destruction of the corpus striatum produced an exaggerated range of reflex times on the contralateral side. These findings support the general concept that the main relationship between higher and lower neural levels is one of dominance of the former over the latter.

ADDISON, Philadelphia.

THE DISSOCIATION OF CORTICAL EXCITATION FROM CORTICAL INHIBITION BY  
PYRAMID SECTION, AND THE SYNDROME OF THAT LESION IN THE CAT.  
SARAH S. TOWER, *Brain* **58**:238, 1935.

The research was designed first to evaluate the consequences of lesions of the pyramidal tract below its last large suprasegmental connection with the pons and then to determine the activity of still surviving suprasegmental projection neurons and corticospinal collaterals by comparison of the effects thus produced with the familiar results of a cortical lesion and by electrical stimulation of the motor cortex after degeneration of its segmental projection tract.

The right pyramid was sectioned at the level of the trapezoid body in ten adult cats. The animals were killed at periods of from three weeks to a year. With one exception every animal presented a similar picture at all times, from two hours after operation throughout the period of survival, even to a year. The effects of the lesion were appreciable only in the contralateral limbs. Homo-

lateral symptoms were absent. The lesion disturbed the normal balance of flexion and extension in progression, the fore and hind extremities being used stiffly, with little or none of the characteristic triple flexion. In any form loss of function was permanent. The extensor mechanisms of the cord were not appreciably affected.

The manifold and enduring losses of function following section of the pyramid may be accepted as those resulting from a corticospinal lesion, the possible contribution of sensory disturbances to the total functional defect having been eliminated. Certain features characterize this loss. First, the effects on flexor and extensor mechanisms are unequal, in conformity with their unequal representation in the motor cortex. Second, phasic movements are impaired, with the preservation of tonic and postural movements. The absence of spasticity and of evidence of release of any lower mechanism is a notable feature in the syndrome.

Six months after the original operation, secondary ablation of the motor cortex was performed. There remained, after the postoperative exacerbation of the old symptoms had passed, slight but definite rigidity in the affected legs, as a new contribution to the syndrome.

The motor cortex of both sides was explored electrically, either prior to ablation or before the animal was killed. The evidence assembled seems to offer an explanation of the absence of spasticity, or of "release" in any form, in the syndrome of a pyramidal lesion and also of the differences between the effect of section of a pyramid and that of cortical ablation. Apparently, excitatory and inhibitory effects of cortical activity are dissociated, in large part at least, at a prespinal level. The excitatory component is then transmitted directly to the spinal cord along the corticospinal tract, while the inhibitory component must be relayed through prespinal centers, to reach the cord finally along other descending pathways.

Anatomic studies showed descending degeneration confined to one pyramid, with a large crossed and a small uncrossed component in the lateral columns of the cord. Ascending degeneration involved the lateral lemniscus on each side and the medial lemniscus chiefly of the side of the lesion. This degeneration of the medial lemniscus is ascribed to the commingling of ascending and descending fibers in the pyramid, making this, like the corresponding area in the cortex, a sensorimotor system.

SALI, Philadelphia.

THE ORIGIN OF THE BERGER RHYTHM. E. D. ADRIAN and K. YAMAGIWA, *Brain* **58**:323, 1935.

In a recent paper Adrian and Matthews (1934) discussed the origin of the Berger rhythm, the characteristic oscillation of electric potential on the surface of the head reported by Hans Berger in 1929. It consists of a series of waves with a frequency of about 10 a second and an amplitude of from 0.05 to 0.1 millivolts, appearing when the subject is at rest with the eyes closed and disappearing when the eyes are opened or the attention is fully engaged. Berger had shown that the potential waves originate in the brain and had made a detailed study of the factors which influence them. Adrian and Matthews repeated and confirmed many of Berger's observations but offered a different interpretation of the rhythm. This is based on the view that the activity responsible for the potential waves is confined to the occipital lobes, whereas in Berger's interpretation the whole cortex is involved. The present work was undertaken to supply more definite evidence on this question, since it is of critical importance in deciding the nature of the rhythm.

Berger stated that every part of the cortex, when active, gives rise to potential waves with a rhythm of 10 a second. The disappearance of the rhythm when the eyes are opened is due to a widespread inhibition, the excitation of a part of the brain causing inhibition elsewhere, with the result that the potential changes, though actually larger in the excited region, are no longer perceptible through

the skull. This view depends on the fact that the potential waves can be detected in almost any part of the scalp. It was criticized by Tonnes (1933), on the ground that the changes in potential, though perceptible elsewhere, appear to rise only from the occipital part of the brain. Adrian and Matthews, for the same reason, suggested that the rhythm is a spontaneous or resting discharge from a large group of neurons in the occipital lobe, neurons mainly concerned with vision. When the eyes are shut, these are left undisturbed and are free to beat in unison at their natural period; when the eyes are opened, the different units must work at different rates, and a synchronous beat is no longer possible.

Adrian and Matthews argued for an occipital origin because the changes in potential are much greater over the occipital part of the head than over the frontal portion. They argued that the active region must be concerned with vision (a) because the rhythm is abolished far more effectively by visual stimuli than by any other kind and (b) because exposing the eyes to a flickering field gives rise to potential waves with the same general distribution over the head but with the frequency of the flicker instead of the usual 10 a second frequency of the Berger rhythm. They found, however, as Berger had done, that the waves recorded simultaneously from two parts of the skull were not always in phase and might change the relation of their phases from time to time. To account for this, they had to assume that the focus of the activity was not at a fixed point but might shift over a fairly wide area at the back of the head. The extent of the area was not decided, but it was recognized that the next step must be to map it as accurately as possible and that no explanation of the rhythm could be considered satisfactory until this had been done.

The present work is concerned primarily with the question of the localization of the focus of activity and the extent of its movement. The distribution of potentials over the head was analyzed by recording simultaneously with three or four pairs of electrodes on the scalp. It was found that the change in potential reaches a maximum in the occipital region, the focus of activity on either side of the midline moving about within an area which extends laterally for from 2 to 2½ inches (5.08 to 6.35 cm.) and upward from the inion for about 2 inches (5.08 cm.). The range of movement varies with the individual person.

By setting up an oscillating potential within the skull in a cadaver and recording from the scalp, it was found that an active region on the surface of the cortex could be located to within an inch by the method in use. Inequalities in the resistance of the skull did not produce appreciable distortion of the distribution of potential in the scalp. Adrian and Yamagiwa conclude that the focus of activity of the Berger rhythm is in the occipital part of the cortex, though it is probable that the activity may sometimes extend beyond the margins of the occipital lobe.

Attempts to influence the position of the focus of activity in other parts of the brain have mainly been unsuccessful. The focus shifts from place to place in a way which agrees with the idea of a spontaneous beat arising within a large group of neurons, and, in fact, the results are consistent with the views of Adrian and Matthews that the rhythm is due to the synchronous activity of neurons which are left to themselves when the eyes are shut.

The failure of the rhythm when the eyes are open is presumably due to increased but asynchronous activity. The rhythm may also fail, however, from diminished activity of the cortex, as in deep sleep or narcosis. Apart from the waves of the Berger rhythm and the occipital waves induced by a flickering field (Adrian and Matthews), Adrian and Yamagiwa found no clear evidence of changes in potential in the scalp due to the activity of the cortex. To give a reasonably large effect, the neurons must act in unison over an area an inch or more in diameter. This can occur normally in the occipital lobe when the eyes are closed, but elsewhere, under conditions which favor an abnormal degree of synchronization, e. g., in epileptiform attacks.

SALL, Philadelphia.

THE INFLUENCE OF THE PITUITARY-LIKE SUBSTANCE IN HUMAN PREGNANCY URINE ON THE MOTOR COMPONENTS OF SEXUAL BEHAVIOUR IN THE SOUTH AFRICAN CLAWED TOAD (*XENOPUS LAEVIS*). H. A. SHAPIRO, South African J. M. Sc. **1**:107 (March) 1936.

The South African clawed toad, according to Shapiro, ceases all sexual behavior in captivity. It therefore forms a suitable experimental animal for the study of factors influencing this behavior. Shapiro injected intraperitoneally an acetone-insoluble extract of the urine of women in an early stage of pregnancy (from one to two months). Three groups of animals were used: (1) a group in which injections were made in both males and females, one hundred and twenty pairs; (2) a group in which injections were made only in females, thirty-seven pairs, and (3) a group in which injections were made only in males, twenty-four pairs. Of the first group ninety pairs (75 per cent) mated, of the second group eleven pairs (30 per cent) and of the third none. No mating was obtained after the injection of extracts of urine from males.

The mating reflex in the clawed toad involves quiescence in the female, clasping of the female by the male for from ten to forty-eight hours, extrusion of the ova by the female and their fertilization by the male. Such a complicated behavior pattern must involve the nervous system. The work of various observers has indicated that the clasping reflex of the male is normally inhibited by a center in the corpora bigemina and that during the breeding season this center is itself inhibited by an endocrine secretion from the testes. This work suggests that the urine of pregnant women contains a substance which inhibits the center in the brain stem of the male, either directly or through the intermediation of the gonads. The action of the substance in the female, producing quiescence, must involve an entirely different mechanism.

Shapiro states that he has obtained identical results with extracts of anterior pituitary, but this work has not yet been reported. MACKAY, Chicago.

THE FRONTAL LOBE AND EQUILIBRIUM. P. DELMAS-MARSALET, *Encéphale* **31**:15 (Jan.) 1936.

Experimental stimulation of the frontal lobe in animals yields the following conclusions: Cephalad to the primary cortical motor centers of the extremities there is a region electric stimulation of which evokes conjugate deviation of the eyes, rotation of the neck and incurvation of the vertebral column. These movements belong to the functions of static equilibration of the body and orientation of the eyes. Traits which distinguish the activity of these centers from the primary motor centers are the higher threshold of electrical excitability, the slowness of the resulting movements, the associated movements evoked—and the sensitivity to bulbo-capnine. The global motor response resulting from stimulation of these centers resembles that from excitation of one labyrinth.

Experimental destruction of one frontal lobe in the dog results in curvature of the neck and trunk with ipsilateral concavity, and in mild disturbances, incoordination in the contralateral paws. There are turning movements toward the side of the lesion. Muskens attributed these movements to lesions in the corpus striatum resulting from injury to the anterior cerebral artery. Delmas-Marsalet destroyed a very small part of the frontal cortex. No abnormal movement resulted until cocaine was injected, whereon the typical curvature, turning movements and crossed ataxia appeared. The lesion was so minute that it could not affect the striate bodies. The crossed ataxia is always transitory, lasting a few days, after which, however, it can be revealed by injection of cocaine or by a labyrinthine lesion. Rotation with the animal's head in a horizontal position produced nystagmus in the same direction and of the same intensity as in the intact animal. But the usual postrotatory deviation of the head and turning movements appeared only with rotation toward the side of the injured frontal lobe and were absent with rotation in the opposite direction. Temporary suppression of the labyrinthine

function by injection of cocaine into the middle ear ipsilateral to the injured frontal lobe intensified the curvature of the neck and body and the turning movement. It added ipsilateral ataxia to the crossed ataxia of the paws. Suppression of the contralateral labyrinth intensified the crossed ataxia. In both cases nystagmus was identical with that which occurs in the dog with the frontal lobe intact. Unlike the pigeon and the rabbit, the dog suffers no disturbance in orientation after unilateral destruction of the frontal lobe.

Destruction of both prefrontal lobes results in no turning movements or incurvations, if the lesions are symmetrical. If not, there is a slight turning toward the more injured side. With the animal at rest the trunk is transversely twisted. In walking the paws are held apart. Often the two scapular or the two pelvic limbs advance together. This, with oscillation of the trunk, results in an uncertain gait. Rotation gives the same results as in the normal dog, but the turning movements are feeble. Cocainization of the labyrinths gives the same result in these dogs as in normal animals, except that the turning movement is of increased intensity. These results cannot be explained as the "algebraic sum" of the lesions of the two frontal lobes.

In order to explain the peculiar intervention of the frontal lobe, complementary experiments were carried out. Section of the frontal segment of the corpus callosum resulted in none of the disturbances resulting from lesions of the frontal lobes. A unilateral lesion of the sigmoid gyrus gave only crossed paresis of the limbs with normal labyrinthine responses, except that cocainization of the contralateral labyrinth increased the paresis. Destruction of the head of the caudate nucleus gave the same results as destruction of the ipsilateral frontal lobe except that hypodermic injection of cocaine did not intensify the turning movements. Destruction of one lenticular nucleus differed from that of the caudate nucleus only in that the turning movements were incomparably more intense and that cocainization of the contralateral labyrinth resulted in no turning movement in any direction. Section of one cerebral peduncle caused intense turning movements and curvature toward the lesion. Rotatory and labyrinthine responses have not been studied in connection with the latter lesion. Destruction of one cerebellar hemisphere resulted in ipsilateral dysmetria, hypotonia and ataxia similar to the crossed ataxia characteristic of frontal lesions and, when preceded by a lesion of the opposite frontal lobe, intensified the ataxia. Intravenous injection of bulbocapnine prevented the appearance of turning movements and curvature after lesions of the frontal lobe, as well as that of similar reactions in the normal dog after rotation or cocainization of one labyrinth, and counteracted the effect of hypodermic injection of cocaine but did not interfere with nystagmus.

All these data suggest the existence of a connection between the prefrontal lobe and the crossed cerebellar hemisphere and between the prefrontal lobe and the ipsilateral vestibular nerve. Reactions apparently at variance with the hypothesis of the latter, such as turning movements toward the side of the injured frontal lobe following cocainization of the crossed labyrinth, can be explained as induced by the attitude of the body and neck. Such a reaction was demonstrated in a normal dog by maintaining its neck turned toward the right by means of a plaster jacket. Cocainization of the left labyrinth then resulted in paradoxical turning movements toward the right. The frontal lobe seems to be a postural center for the neck and trunk.

Clinically, the large mass of facts shows that disturbances of coordination resulting from lesions of the frontal lobe can be grouped under four main heads: cerebellar, labyrinthine and postural, praxic and gnostic. Disturbances of cerebellar origin correspond mainly to lesions of the crossed cerebellar hemisphere—dysmetria, adiakokinesis, tremor, ataxia, spontaneous deviation of the limbs on the side opposite the lesion and lateropulsion away from the lesion—and occasionally to those of the vermis—ataxia and asynergia of the trunk and retropulsion. Disturbances due to labyrinthine involvement are reminiscent of those following a lesion of the ipsilateral labyrinth, namely, inclination of the head and body toward the lesion, spontaneous deviation of the index finger and of gait toward the side of

the lesion and a tendency to deviate in the same direction after rotation. Bilateral adiakokinesis and apraxia in walking are forms of apraxia and recall symptoms of disturbance in the corpus callosum. Gnostic symptoms are vertigo, false impressions of bodily displacement, lack of perception of certain bodily displacements and disturbances in spatial orientation and the postural image of the body. These symptoms can occur separately or in various combinations, which explains the great variability of syndromes of the frontal lobe.

Topographically there are three main syndromes: superficial, deep and mixed. The superficial syndrome is subdivided into three regional subheads: The pediculofrontal syndrome corresponds to a lesion of the foot of the first and the second frontal gyrus and comprises symptoms of involvement of the crossed cerebellar hemisphere in the pelvic extremity, for the first frontal gyrus, and in the scapular extremity for the second frontal gyrus. There may also be bilateral apraxia in erect walking. The mediofrontal syndrome corresponds to a lesion of the middle parts of the three frontal gyri and consists of ipsilateral labyrinthine symptoms and sometimes spatial disorientation. The telefrontal syndrome corresponds to a lesion of the most oral region of the frontal lobe and consists mainly of spatial disorientation. The deep frontal syndrome corresponds to a large central lesion of the frontal lobe, acting on the corpus callosum and even the opposite frontal lobe. Its symptomatology is not clearly delimited. It seems to include intense, massive, bilateral astasia-abasia and sometimes spatial disorientation, inversion of evoked deviation of gait following rotation and anteropulsion or retropulsion. A mixed frontal syndrome results from combinations of the preceding syndromes. It tends to bilateralization of the symptoms with unilateral lesions. This sketch of a classification, "far from constituting a formal law, pretends simply to translate a statistical frequency."

Many lesions of the frontal lobe do not result in any disturbance of coordination. This is sometimes due to concomitant lesions of the primary motor centers. In the absence of voluntary movement incoordination cannot be observed. More often, the absence of incoordination is due to compensation by other parts of the neuraxis. Scopolamine can make apparent latent incoordination, as cocaine does in the dog.

Architectonically, the pediculofrontal area is constituted by cortex type 1 of von Economo; the mediofrontal area by cortex type 1 in the first frontal gyrus and by cortex type 2 in the second and third frontal gyri, and the telefrontal area, by cortex type 3. The telefrontal area resembles the region of the first temporal gyrus, which is believed to receive the vestibular path. This resemblance, with physiologic and clinical considerations, support the hypothesis that the mediofrontal and telefrontal areas are connected with the vestibular path and the mediofrontal also with the cerebellum.

The connections of the prefrontal lobe involved in its function of coordination seem to be the frontopontile, the thalamofrontal, the pallidofrontal and the frontospinal tracts. The globus pallidus is probably a relay station for the ascending vestibular path. Serial sections of the neuraxis of a dog in which the anterior frontal *carrefour* was destroyed showed ipsilateral degeneration in the centrum ovale, the segment of the corpus callosum joining the second, third and fourth gyri arcuati, the inferior part of the anterior segment of the internal capsule, a few fibers in the head of the caudate nucleus, a small bundle in the external capsule, part of the inferior zone of the posterior segment of the internal capsule, the lateral medullary lamina, the anterior part of the posterior and the lateral nucleus of the thalamus, scattered fibers at the origin of the pes pedunculi and in the juxtanigral part of the pes, a few fibers in the medial geniculate body, the bundles ending in the pontile nuclei in the ventral level of the pons and scattered fibers in the anterior pyramid at the level of the medulla. The last-mentioned fibers follow the corresponding pyramidal tract through the first 3 or 4 cm. of the spinal cord. Atrophy of ganglion cells was observed in the lateral nucleus and the anterior part of the posterior nucleus of the thalamus and in the corpus hypothalamicum and, to a slight degree, in the putamen and the substantia nigra.

LIBER, New York.

POSITION OF THE FEET IN THE STATION OF MAN: RELATIONS OF THESE PHENOMENA TO THE STATE OF THE VESTIBULAR APPARATUS. L. LITVAK,  
Rev. d'oto-neuro-opht. 14:176 (March) 1936.

Litvak has shown previously that there are three successive phases of reaction which prevent a standing person from falling when he is pushed: global contraction of the musculature of the legs, raising the edge of the foot corresponding to the direction of the push and the reaction of hopping. The optimal position of the feet in the preservation of equilibrium is the usual one of the feet side by side, with the points slightly deviated. The least favorable attitudes of the feet are: (1) the frontal, with the feet in the frontal plane, the heels together and the feet everted as much as possible, and (2) the sagittal, with one foot placed directly in front of the other in the sagittal plane. Examination of patients with disorders of the nervous system by testing their falling reactions with the feet in these unfavorable positions offers a sensitive method of determining slight and precocious instability. Twenty-three patients were thus studied. They were divided into two main groups: (1) patients with diffuse lesions of the nervous system, such as disseminated sclerosis, influenzal encephalitis, postinfluenzal labyrinthitis and syringobulbia, and (2) patients with verified cerebral tumor, located in the cerebellum, the cerebellopontile angle and the frontal and the temporal lobe, respectively. In all cases studies were made of the upright station when the feet were in the ordinary position and when they were in the frontal and sagittal attitudes. The tests of Romberg and Sarbó were also applied. It was determined that in cases in which static disturbances were well marked, change of the attitude of the feet was immediately followed by disequilibration. In unilateral disturbances of station disequilibration was most manifest when the feet were in the sagittal position. The patient with such a lesion fell toward the side of the focus, especially if the foot on the diseased side was in front of the other. In bilateral disturbances of station disequilibration was most marked when the feet were in the frontal position; the patient then fell backward. If the usual method of examination revealed no static disturbance, change of the position of the feet was usually followed by loss of equilibrium to a certain degree and a tendency to fall, especially if the patient was given a slight push in the direction of the presumed direction of falling. All the facts elicited by these studies demonstrate that the station of man depends on the position of the feet and that this is one of the most important factors in maintaining the upright posture. The mechanisms that form the basis of this factor are not voluntary but reflex in character. By changing the position of the feet and thus causing new relations between the terminal articulation and the whole limb and between the limb and the median line, the conditions that permit a normal distribution of tonus to the extremities are altered. From this arise disturbances of station and a condition of unstable equilibrium, which is revealed especially by a slight push.

DENNIS, San Diego, Calif.

DISTANT EFFECTS OF HIGH FREQUENCY CURRENTS ON NERVES. B. DANIELEWSKY  
and A. WOROBJEW, Arch. f. d. ges. Physiol. 236:440, 1935.

The authors studied the irradiation effects of alternating currents with wavelengths of from 400 to 600 millimicrons; the electrodes were not in contact with the nerves but were placed at a distance of from 40 to 400 cm. The excitability of the nerves was tested by direct faradic or by mechanical stimulation. The experiments were performed on frogs, rabbits and cats. It was shown on the nerve-muscle preparation of the frog that irradiation with such currents increased the excitability, that subliminal test stimuli became effective and that contraction of the muscles was increased. Such an effect was observed even if the irradiation lasted only from 0.2 to 0.3 second. After the irradiation the excitability quickly returned to its initial value. After intense irradiation the excitability of the nerves was lowered. The effect of the irradiation was markedly increased when the nerve-muscle preparation was grounded. In rabbits and cats the sciatic nerve

was severed, and the distal end was irradiated. The changes in the excitability were the same as for the frog. The reflex reactions of decapitated frogs were rarely increased by irradiation; usually depression of the reflex irritability was noticed.

SPIEGEL, Philadelphia.

### Neuropathology

DIFFUSE CORTICAL CONTUSION OF THE OCCIPITAL LOBE. C. B. COURVILLE, Arch. Path. 20:523 (Oct.) 1935.

Contusion is one of the more common traumatic lesions of the brain. While there is difference of opinion as to the exact mechanism of its production, it is generally agreed that in most instances it is a contrecoup effect. Two notable exceptions to this rule are cerebral contusion which occasionally results from a depressed fracture of the cranial vault and cerebellar contusion secondary to a linear fracture of the occipital bone, which usually runs near or into the foramen magnum.

The nature of the contusion depends largely on the anatomic relationship of the brain to the internal contour of the skull in the region affected. The shape of the contusion is also affected somewhat by the internal structure of the brain, particularly by the arrangement of the bundles of white fibers in the affected part. Three anatomic types of contusions are thus produced, the first with two subtypes: (1) the wedge-shaped temporofrontal contusion with (a) subfrontal and (b) antero-lateral temporal subtypes, (2) the patchy and superficial dorsolateral contusion usual in the opercular cortex and (3) the diffuse cortical contusion of the occipital lobe.

It is the purpose of this study to draw attention to the essential features of a type of contusion which has not been described in the literature. Certainly, it must be familiar to coroner's pathologists in large metropolitan centers, but writers on the subject have not distinguished it from other types of cerebral contusion. The lesion appears as a diffuse reddish brown discoloration, due to the presence in the cortex of myriads of petechial hemorrhages. The lesion has occurred invariably in the posterior portion of the cerebral hemisphere. The area involved varies considerably in size, from small patches of discoloration in the cortex, often at the depth of a sulcus, on the one hand, to a change in the cortex of the entire occipital lobe, on the other.

From a study of the clinical histories and observations at autopsy in a series of cases, it was found that diffuse occipital contusion occurs in persons over 40 years of age, usually several days after the injury has taken place. It occurs after blows on the head, falls and automobile accidents. It may occur without fracture of the skull; there is no definite anatomic relationship between fracture, when present, and the contusion. The scalp wounds occur likewise over the posterior half of the head. First glance suggests that some regional anatomic peculiarity is responsible for this type of lesion. The absence of superficial lacerations of the cortex in the affected area, such as occur when the bruise is due to contact with bone, and the occurrence of such lesions along the free margin of the tentorium suggest, furthermore, the possibility that the arrangement of the dural reduplications may play an important rôle in the production of the diffuse contusion.

Diffuse contusion of the occipital lobe results from two types of mechanical disturbance: 1. The lesion may be primary and acute, resulting from forcing the occipital cortex against the falx or the tentorium, when the head in motion strikes some relatively immovable object. The force of the blow is expended on the sides or the top of the head. Although in the primary type the contusion of the brain is usually on the same side as that of the injury to the scalp, it occurs on the opposite side of the occipital lobe and is therefore a contrecoup. 2. The secondary type is the result of local pressure by an expanding lesion, such as edema or subdural or intracerebral hemorrhage. In this type there is no necessary

relationship between the side of the original injury and that of the contusion. In any case the lesion is essentially a diffuse hemorrhagic softening of the cortex resulting from a rupture of small cortical veins incident to the sudden reversal of current in these vessels in the primary type, or to persistent and increasing obstruction by continued pressure in the secondary type. Microscopically, the cortical and subcortical tissues are infiltrated with blood. The softening and disintegrating tissues are ultimately filled with compound granular corpuscles. The appearance of the ultimate lesion is unknown, since no example has as yet been studied.

WINKELMAN, Philadelphia.

**CONGENITAL MALFORMATION OF THE CEREBRUM ASSOCIATED WITH MICROCEPHALY.**  
CYRIL B. COURVILLE, Bull. Los Angeles Neurol. Soc. 1:2 (March) 1936.

Courville reports the case of an infant aged 17 days with a small head (31 cm. in circumference), closed fontanel, cleft lip and palate, absence of nasal septum and almost constant convulsions and nystagmus. Death occurred at the age of 61 days. Necropsy revealed that the cerebrum occupied only the anterior one third of the cranial vault. The posterior two-thirds was occupied by a thin-walled sac, the cavity of which opened directly into the cerebrum. The aqueduct of Sylvius lay open in the floor of the sac, and the thalamus and corpora quadrigemina were on either side of the opening. The cerebrum was a thin shell of cortex with a few external markings, no corpus callosum and only a tendency to divide into two hemispheres. The leptomeninges were thickened at the base and involved the cranial nerves. The olfactory bulb, olfactory tract and olfactory trigon were absent bilaterally. The pons was small; the pyramidal tracts were absent, and the cerebellum was relatively normal in size. Courville remarks on the occurrence of convulsions in the absence of motor fibers in the brain stem. He considered the condition a developmental anomaly dating from early embryonic life.

MACKAY, Chicago.

**MECHANISM OF INTERNAL HYDROCEPHALUS IN SPINA BIFIDA.** DOROTHY S. RUSSELL and CHARLES DONALD, Brain 58:203, 1935.

The frequent association of hydrocephalus with spina bifida has been observed for centuries, but no explanation of this association has yet proved generally acceptable. Russell and Donald offer a mechanical explanation of the production of communicating hydrocephalus in a series of cases of meningocele. Ten cases were studied. Internal hydrocephalus was present at birth in all but two instances. Of the eight cases in which hydrocephalus was present, two were of the noncommunicating type and three of the communicating type, and in the three remaining cases the type was not determined. In all ten cases a remarkable malformation of the hindbrain was observed. A tongue of variable length, consisting of cerebellar tissue and the greatly elongated medulla oblongata, protruded downward into the spinal canal. It overlapped and compressed the upper segments of the cervical portion of the cord, distending the dural theca in this neighborhood and filling the foramen magnum. The cavity of the fourth ventricle extended ventrally into this tongue, lying between the cerebellar and the medullary component. The spinal cord appeared abnormally small, and the cervical roots always ran in a cephalic direction to reach their exits through the dura mater. Hydromyelia was commonly present in a variable number of consecutive segments in the cervical and thoracic portions of the cord. There was conspicuous hypoplasia of the cerebellum. The pons and the cranial nerve roots arising from the pons and the medulla were greatly elongated.

This curious maldevelopment was first described by Arnold (1894) and was subsequently studied by Chiari (1895), Solovtsoff (1901) and Gredig and Schwalbe (1907), the last-named authors describing it as the Arnold-Chiari malformation.

The relation of the malformation to hydrocephalus is explained as follows: The elongated fourth ventricle extends for a considerable distance below the

foramen magnum; it follows that if the foramina of Luschka and Magendie are patent, the cerebrospinal fluid escapes into the subarachnoid space within the vertebral canal. The plugging of the upper cervical part of the canal by the Arnold-Chiari malformation is likely to hinder any upward flow of fluid into the subarachnoid channels within the posterior fossa, into which it passes normally on its way to escape through the cranial arachnoid villi. According to the experiments of Dandy and Blackfan, the greater proportion, from three-fourths to four-fifths, of cerebrospinal fluid is absorbed from the surface of the brain, and from one-fourth to one-fifth only, from the spinal canal. If this estimate is accepted, it follows that occlusion of the foramen magnum in cases of spina bifida will lead to damming back of cerebrospinal fluid in the ventricular system and hence to internal hydrocephalus. Evidence can be advanced in support of this hypothesis. In two cases in which death was imminent, a suspension of india ink was introduced into the lateral ventricles, and the distribution of the particles was examined at necropsy. There was a profuse deposit of pigment throughout the ventricular system and in the subarachnoid space of the spinal canal below the level of the Arnold-Chiari malformation. Above this level a very small or moderate amount was visible at the base of the brain, and a very little, in the sulci over the cerebral convexities. In two other instances there were ascending purulent leptomeningitis and pyocephalus following infection of the tissues at the site of the spinal defect. Examination showed a severe purulent infiltration of the spinal meninges up to the level of the Arnold-Chiari malformation, but above this level the inflammatory reaction was confined mainly to the ventricular system, where conspicuous pyocephalus was present.

Hydrocephalus has also been observed in some cases of meningomyelocele. Russell and Donald studied one case in which there was no associated hydrocephalus. In this case a type of malformation similar to that described in the cases of meningomyelocele with hydrocephalus was presented, but to a far less severe degree. This suggests the possibility that greater degrees of the malformation may be the cause of the hydrocephalus which complicates meningomyelocele in some instances.

Examination in two cases of spina bifida occulta in which hydrocephalus was absent disclosed no abnormality in the brain stem. SALL, Philadelphia.

**CYSTIC EPENDYMOCTOMA OF THE THIRD VENTRICLE.** STATE DRĂGĂNESCO and O. SAGER, *Encéphale* 30:512, 1935.

A case is reported to illustrate the psychic disturbances which may result from a tumor of the third ventricle. The case was that of a woman physician aged 55. In 1930 an atypical abdominal syndrome with headache led to a diagnosis of appendicitis. Operation showed perityphlitis with adhesions. Headache persisted. There was change of character, with mannerisms, irascibility and weakness of memory. Three months later attacks of somnolence with oneiric delirium, adiposity and polyuria appeared. In spite of negative Wassermann reactions of the blood and spinal fluid, antisiphilitic treatment was undertaken and resulted in improvement lasting seven months. Headache yielded to injections of a hypertonic solution of dextrose. Later the symptoms returned. During attacks of somnolence the photopupillary, patellar and achilles reflexes disappeared. Both optic nerve heads showed slight pallor. The patient died in coma with hyperthermia.

Autopsy of the brain only was performed. In the third ventricle a tumor arising from the infundibulum was implanted on the inner surface of a cystlike sac formed by reduplication of the ventricular ependyma. The tumor was composed of papillae, each of which comprised an axis of vascular connective tissue covered with pluristratified, polygonal or cuboidal epithelial cells. In places the cells were joined by protoplasmic bridges, like prickle cells. The epithelial layer was continuous with that of the ependymal sac. The tumor was therefore diagnosed as epithelial ependymocytoma. The peculiar disposition of the ependyma can be explained only as an embryonal malformation. The nuclei of the tuber

had disappeared completely, which probably explains the diabetes insipidus and adiposity. Slight lesions of the juxtafornical nuclei may explain the somnolence and oneiric delirium. The dorsal surface of the optic chiasma was demyelinated.

LIBER, New York.

**TUMOR OF THE BRAIN IN A MONKEY.** A. P. SELLHEIM, J. belge de neurol. et de psychiat. **36:**240 (April) 1936.

A cercopithecus monkey aged 4 years came from the Congo in 1928. He was excitable and aggressive. In 1929 he had two convulsive seizures and lost consciousness; at times he became maniacal. In 1930 he started jerking and biting his left lower limb, which had a spontaneous tremor. Conditioned reflexes were established with difficulty and were not stable. In March 1931 the monkey became quiet and sat with his head lowered for long periods at a time. His gait was staggering, and there was often a generalized tremor. On the day after these observations tests indicated that the monkey was blind. The pupils were dilated and inactive; a Babinski reflex was present on the left side, with absence of the abdominal reflexes. Muscular rigidity prevented examination of the tendon reflexes, and the monkey did not cry out. The convulsive attacks persisted up to the time of death. At autopsy a tumor of the brain was observed on the external surface of the right occipital lobe, measuring 4 by 3 cm. Microscopically it was an atypical glioma, formerly called a gliosarcoma.

FREEMAN, Washington, D. C.

**CONTRIBUTION TO THE LOCALIZATION OF ARTERIOSCLEROSIS IN THE VESSELS OF THE BRAIN.** JOSEPH DÖRFLER, Arch. f. Psychiat. **103:**180 (March) 1935.

Dörfler studied a large number of cases of arteriosclerosis for the purpose of determining the most frequent localization of this condition in vessels of the brain. In accordance with Spatz, he divides the arteries into: (1) stems (the internal carotid and the vertebral artery), (2) limbs (subdivisions of the stems while they still are in their intrameningeal course) and (3) branches (all the arteries and arterioles within the brain substance). In forty-seven patients with advanced arteriosclerosis of the vessels of the brain whose ages averaged 66 years, the sclerosis was observed primarily in the stems; only in nine patients were the limbs affected whereas little change was seen in the branches. Of one hundred and twenty patients with general arteriosclerosis on whom autopsy was performed, involvement of the intracranial vessels was shown in ninety-two. They were all older than 40. The other twenty-eight patients were below this age. In twenty-five patients the internal carotid artery was the only vessel affected. In fifty-one persons the change was observed also in the limbs. In fifteen persons the limbs were affected equally as seriously as the internal carotid artery. The microscopic changes were most frequently localized in the stems and were observed in some cases in patients as young as 17 and 19 years of age. In the internal carotid artery the changes were chiefly in the parts of the artery which either are fixed by the meninges or lie against the underlying bone. Of the four curvatures of the internal carotid artery, the third and fourth are most frequently affected. The intracerebral vessels are affected least of all, and only in persons of the most advanced ages.

W. MALAMUD, Iowa City.

**LATE INJURY OF THE HUMAN BRAIN RESULTING FROM ROENTGEN IRRADIATION.** T. MARKIEWICZ, Ztschr. f. d. ges. Neurol. u. Psychiat. **152:**548 (April) 1935.

The anatomicoclinical details in an unusual case of late injury to the human brain due to exposure to roentgen rays are reported, the first symptom appearing one and one-half years after the last irradiation of the head. The patient was treated three times in 1925 with high voltage roentgen radiation for convulsive attacks, and once in 1928. The details of the dosage were not known. On the patient's second admission to the hospital a large roentgen ulcer of the scalp,

with exposure of the periosteum, was noted. Autopsy showed a large roentgen ulcer of the occipital region, atrophy of the bones of the skull, chronic dermatitis of the head, face and lower limbs, atrophy of the skin in this region secondary to exposure to roentgen rays, healed tuberculosis in the apexes of both lungs, brown atrophy of the heart and liver and pulmonary emphysema. Gross examination of the brain showed thickened meninges in the region of the frontal poles. The occipital lobes appeared soft, hemorrhagic and somewhat indented. The vessels in this area were dilated. There were extensive areas of hemorrhagic softening in both occipital lobes, more marked on the left side and especially in the white substance, with occasional involvement of the cortex. The same tissue alterations extended anteriorly as far as the rolandic fissure, though they were less intense. Histologic examination showed extensive necrosis of the brain tissue, with the neural parenchyma intact only at the periphery. The larger areas of necrosis were composed of a confluence of multiple hemorrhagic areas. An occasional isolated focus was seen in the white substance and the cortex, especially on the right. The absence of glial reaction was noteworthy. A homogeneous substance throughout stained reddish yellow with the van Gieson stain. Occasional gitter cells were seen, though the process of clearing away appeared minimal and feeble throughout. Long-standing and recent hemorrhages were seen in all the sections. The blood vessels in these affected areas showed marked hyaline degeneration. There was no relation between the intensity of the process and the presence of the vascular lesions. Similar changes in the vessels were seen at a distance from the necrotic areas. In some areas there were swollen vascular walls continuous with the homogeneous colloid substance observed in the tissues. Occasionally early thrombosis was also seen. In a few vessels there was intimal proliferation. The meninges over the necrotic areas were filled with macrophages and an increased amount of fluid. There was fibrous thickening of the pia. The colloid change was also noted in some of the meningeal blood vessels, though the homogeneous substance was not observed in the surrounding meningeal tissues. Markiewicz calls attention to this homogeneous substance and points out its similarity to the coagulation necrosis of Spielmeyer and its resemblance to the colloid degeneration of the vessels described by Alzheimer. He considers the vascular changes, the necrosis due to circulatory impairment and the homogeneous substance in the parenchyma as reactions to the same noxious agent, in this case the roentgen ray.

Markiewicz concludes that this case is one of late injury to the brain as a result of roentgen treatment. He points out the similarity of the observations in this case and the results of recent experimental work by Scholz. Late sequels of irradiation have been noted in other organs, especially the skin.

SAVITSKY, New York.

### Psychiatry and Psychopathology

THE LETHAL POWER OF THE EMOTIONS. DONALD GREGG, *Ment. Hyg.* **20**:30 (Jan.) 1936.

A study of the mortality incidence among physicians, members of the community and patients committed as insane to Massachusetts state hospitals suggests that the greater the emotional element involved in a disease the higher the relative mortality will be among persons capable of physiologic emotional reaction as compared with those less capable of this response. In general, the ratios between the incidence for normal physicians as a group and that for the community at large are close. The relatively higher incidence of suicide among physicians is due, perhaps, to the materialistic philosophy held by many of them.

Deleterious physiologic emotional reactions are predominantly endocrine or autonomic in source. Increasing emotional strain must be reduced by diminishing the frequency, intensity or continuity of emotional stimuli; by slackening the pace; by avoiding excessive specialization, thereby lessening dependence on others; by

increasing knowledge of facts and wisdom in applying them, and by acquiring a philosophy and a faith to take the place of that which increased, but still fragmentary, knowledge has shaken or destroyed. As Balzac said, "To kill the emotions and so live to old age, or to accept the martyrdom of our passions and die young, is our doom."

DAVIDSON, Newark, N. J.

FOUR YEARS OF STUDENT MENTAL-HYGIENE WORK AT THE UNIVERSITY OF MICHIGAN. THEOPHILE RAPHAEL, *Ment. Hyg.* **20**:218 (April) 1936.

The results of four years' operation of a full time, professionally directed mental hygiene unit serving a large university indicate that this need may be met by the construction within the total welfare organization of a specially trained and comprehensive personnel division to deal with the simpler problems of the entire student body, together with a psychiatric unit reserved for consultation service and for managing conditions requiring major psychotherapy. Students in need of help were found during general physical examinations and were referred to psychiatric workers for history taking and often for therapeutic interviews. Psychiatrists made further investigation, assigned students with simpler conditions to workers and themselves cared for the more complex problems.

About one half of the patients seemed to show questionable stability of personality, and one-fourth had a physical handicap, the most common being visual defects, malnutrition and gynecologic disturbances. The results indicate that extremely prolonged care is usually not necessary. The relatively small but important fraction of major conditions in this group should be detected and treated promptly. In most of the problems of *simple* maladjustment much may be expected of psychotherapy.

The presenting factors in students' problems seemed to be: (1) a pronounced tendency to excitability and tension, (2) worry over school work, (3) poor orientation in the university as part of a total life situation and (4) overimpulsiveness. The most fundamental factors were: (1) immaturity, (2) inadequacy, (3) oversensitivity and (4) instability. In some instances treatment could not be completed; in others answering questions and giving advice gave relief by enabling the student to make necessary decisions; in the majority of cases, however, adequate therapeutic contacts led to correction or marked improvement of difficulties. About three fifths of the patients were graduated or continued attendance at the university. About one half of the students in the entire group achieved academic or extracurricular distinction.      DAVIDSON, Newark, N. J.

NEW DATA RELATIVE TO THE INCIDENCE OF MENTAL DISEASE AMONG JEWS. BENJAMIN MALZBERG, *Ment. Hyg.* **20**:280 (April) 1936.

Contrary to popular opinion, Jews are less liable to mental disease than most other groups. This conclusion was reached by Malzberg, after a study of the statistics for patients on first admission to institutions for the treatment of mental disease in New York, Massachusetts and Illinois. The greatest differences are found in patients with alcoholic psychoses and dementia paralytica. In respect to manic-depressive psychosis and dementia praecox, the differences between foreign Jews and all white foreign-born persons do not appear significant, though the rates for male Jews are slightly less than those for the males of the second group. Foreign female Jews have a higher rate of mental disease than foreign male Jews, whereas among all foreign-born patients males have a higher rate than females. Almost two thirds of the total number of Jews on first admission had dementia praecox and arteriosclerotic and manic-depressive psychoses. The "functional" psychoses are relatively more prevalent among Jewish patients with mental disease than among all the foreign white patients.

In comparing the foreign-born Jews with the native population, Malzberg finds that male Jews have lower rates than native males; the best figures available indicate, however, that for Jewish females the rate of mental disease is higher than that for native females. Comparison of foreign Jews with the foreign white population of New York State shows that Jews have less than their proportionate amount of mental disease. DAVIDSON, Newark, N. J.

MARITAL STATUS IN RELATION TO THE PREVALENCE OF MENTAL DISEASE. BENJAMIN MALZBERG, *Psychiatric Quart.* **10**:245 (April) 1936.

That married persons have a lower rate of insanity than single persons is grossly apparent from statistics. These statistics are defective, however, because they fail to account for the differences in age and specific psychoses. To correct this defect, Malzberg made a careful statistical analysis on the basis of age, type of psychosis and marital status of 28,000 patients on first admission to hospitals for the treatment of mental diseases in New York State. This confirms the general conclusion and indicates that single persons have a significantly greater incidence of psychosis than married persons. Exceptions to this are alcoholism and dementia paralytica in females. Presumably, this is due to the greater social restraint placed on unmarried women with respect to exposure to syphilis and alcohol. While Malzberg is inclined to agree that the lower rate of psychosis among married persons is the result of the patients being recruited from a group which is mentally more stable than that which supplies celibates, he is reluctant to deny categorically that the marriage status itself may have something to do with the mental health. He suggests that family life may have an immeasurable and imponderable influence on the mental and emotional stability of its practitioners which is reflected in their lower rates of insanity.

DAVIDSON, Newark, N. J.

INTROJECTION AND SCHIZOPHRENIA. CLIFFORD ALLEN, *Psychoanalyt. Rev.* **22**:121 (April) 1935.

Although projection has been studied somewhat exhaustively, its counterpart introjection has not aroused the same amount of interest. It is an important mechanism in melancholia and schizophrenia. The reason for its neglect lies in the fact that introjection is frequently concealed by the presence of a secondary projection. This may occur in the following way: A man introjects the personality of his mother; he begins to feel feminine and thinks people are commenting on him; soon he hears people saying he is a woman and builds up delusions that there is a plot against him. Superficially, the illness appears to depend on projection, whereas the fundamental mechanism is the original introjection.

Introjection is usually an exact mechanism so that when one person introjects another, every characteristic is absorbed and the most minute mental and physical peculiarities are reproduced, with amazing accuracy. Introjection is entirely an unconscious mechanism. Mimicry, which is its conscious counterpart, is never so persistent nor so exact. Allen accepts Freud's view that when the unconscious is forced to forfeit some beloved object, it is unable to do so unless it retains a replica. The unconscious, according to this view, is the catacomb of dead loves.

Allen reports five cases. Case 1 is that of a man aged 23 who complained that he was the victim of a plot, that he was called womanish and that horrible threats were uttered against him. These threats were so real that he attempted suicide on two occasions. Analysis revealed strong incestuous attachments to his mother and sister. He had experienced a number of sexual acts with his sister, one of which had led to actual intercourse. He had slept with his mother and sister in one bed until the age of 21. The terrific attraction which his sister had for him is shown by the fact that he became bitterly jealous when she started keeping company with other men and constantly quarreled with her, ostensibly because he was fearful lest she should come to moral harm.

The first psychotic symptoms appeared at the age of 18 years, when, at the instigation of his mother, he had to give up the girl he loved. He thought he heard "comments" on the street. He imagined that people thought he was girlish and feminine on the left side. (It is interesting that the symbol of right for masculine and left for feminine permeated his whole unconscious life.) He examined himself in a mirror and thought that he looked girlish on that side. People also seemed to be saying that he was thin. He gained the impression that his left arm and hand were thinner than normal. The clue to these comments is shown by the fact that his mother had an old injury which crippled her left side. Moreover, she was fat. It is clear that the patient introjected his mother's personality and felt that he resembled her physically. He actually insisted that he was crippled on the left side and was surprised that on physical examination no difference could be found. That this was not acceptable to his unconscious is shown by the fact that the hallucinations commented unfavorably on his left-sided femininity. He evidently projected his guilt, dependent on femininity, and this projection was based on introjection, the latter again being dependent on the fact that he must have felt he was abandoning his mother for a stranger. Faced by this psychologic dilemma, he absorbed his mother, succeeded in retaining her and yet kept one half of himself (the right half) for loving another.

At the age of 23 he fell in love with a girl but made no advances to her. His mother died shortly after, and he steadily grew worse; finally, he was admitted to a hospital. Shortly after becoming hallucinated, he consumed his semen after masturbation, rationalizing it as an attempt to repair the damage which he had done himself in this act. His hallucinations stated, however, that he had destroyed a life by this behavior and his own life was forfeited. This punishment was not without significance. In the patient's unconscious he was not one person but two—his mother and himself. Therefore in putting sperm into himself, he was also putting it into his mother, using the mouth symbolically as a vaginal orifice. But whose life had he destroyed that he must forfeit his own? Allen thinks that the true explanation lies in this: The patient felt that if he was permitted to fertilize his mother, he must have disposed of his father, and the life he destroyed was therefore his father's. His dreams reveal frankly hostile wishes toward the father and a savage desire to wrench the mother from him.

Case 2 was that of a man aged 40. His attempts to find a suitable mate led him into a confused mental state. He felt that persons were touching their faces in a peculiar way when he passed them on the street. Before he left the office, he attempted to buy a revolver in order to shoot a man who had dominated him. There developed feelings of influence. He wondered whether his sister had conceived. About this time his mother suffered from right hemiplegia. He identified himself with his sister and said he felt as though he was a woman in the personality of his sister. Later he felt he was paralyzed in the same way as his mother. About this time he thought that his mother was controlling him. The slow development of the patient's illness coincided with his love affairs. He had never been successful in his love life. For some unconscious reason, he felt that marriage was sinful. While in the army, he once fainted on parade and, as he was recovering, heard a remark about Napoleon being an epileptic. This produced a series of fits, which always ceased when things went well but started again at the least suggestion of an unpleasant situation. It is interesting that in his amorous adventures he had a penchant for school teachers and nearly became engaged to seven. He discovered that his attraction to teachers was based on the fact that they have a combination of male and female attributes. They are women of authority and thus represent a fusion of the father and the mother imago. It is obvious that the patient retained an infantile attitude and had never emancipated himself from his parents, for which reason he sought a substitute in a mate who was feminine and yet wielded authority. When the effort proved unsuccessful, he introjected his sister and his mother.

Case 3 concerns a young married woman who complained of one symptom only, that she had no anterior wall to her abdomen. While she admitted that one could see an anterior wall, she would not admit it was there. The reason for this curious delusion was obvious, when one learned that she had given birth to a child with ectopia ventris; there was practically no anterior wall. It was apparent that she had introjected a love object, her child. When she became pregnant the year before her admission to the hospital, she made every effort to abort. After the child was born, she wanted the child, in spite of previous efforts at abortion. After confinement she had anxiety dreams of rats, mice and burglars. Two months after confinement she had an attack of hysterical paralysis, which had to do with the visits of her husband and mother, both of whom she disliked. A year after the birth of the last child, she became mentally ill. She felt as though she were dying, as though the front of her "stomach" was broken. During this period prior to admission to the hospital, she never thought of the child with ectopia ventris. On admission to the hospital she insisted that her abdomen was wrong and then qualified the statement by asserting that the anterior wall of the abdomen was missing. The identification with the child was overdetermined and was dependent on both repression and introjection. The patient was trying to become a child—moreover, a particular child. Her fear of dying and her attempted suicide possibly represented her feelings toward the child which she introjected. The fact that the patient never had any hallucinations or other signs of secondary projection may be of prognostic significance that pure introjection may not be of evil import as when it is combined with projection.

After presentation of the five cases Allen discusses the dependence of introjection on the oral stages, especially the second. This is found when the young child wishes to incorporate his love object into himself by eating ("I could eat you"). Allen, however, failed to find the traits of characters usually assigned to oral eroticism in his patients and therefore reserves judgment until further material clarifies it.

In contrasting introjection in states of depression of the manic-depressive type and in schizophrenia, Allen states that in melancholia the patient feels the emotion which he formerly felt directed toward the introjected object but that this emotion is now directed toward himself and may be so strong as to force him to commit suicide, in order to destroy the unconsciously hated person within. The person with schizophrenia is much more conscious of the introjection—he feels symptoms, "paralysis" for example, which indicate the nature of the introjected object. Unlike the person with melancholia, he feels little emotion, and the constant moaning and whining of the former are absent in his case.

KARPMAN, Washington, D. C.

THE LOGIC OF EMOTIONS AND ITS DYNAMIC BACKGROUND. FRANZ ALEXANDER,  
Internat. J. Psycho-Analysis 16:399 (Oct.) 1935.

Just as logical thinking is based on intellectual syllogisms, the logic of emotions consists of a series of emotional syllogisms. The logic of thinking is the crystallized product of external, and the logic of emotions that of internal experiences. As such, the logic of emotions is more ancient than logical thinking, which probably explains its ability to overpower intellectual processes. It is justifiable, then, to call emotional causal relationships the logic of emotions, for they are as binding as those intellectual relations which are based on logical thinking. For example, if A has insulted B, it is as logical for B to hate A as to prove logically that two plus two equals four.

In many emotional syllogisms a certain polarity constitutes a common and striking feature. The expression of a tendency is likely to provoke and strengthen its polar opposite: For example, suffering increases a tendency toward gratification and vice versa; indulgence in a pleasurable gratification increases guilt, which then gives rise to an inhibitory reaction against the gratification. Furthermore,

extreme masculine aggressive competition is likely to strengthen the polar opposite passive female tendency; passive female tendencies, again, by wounding the masculine narcissism, stimulate the masculine attitude. Dependence stimulates the opposite tendency toward independence, effort and struggling increase again the polar opposite wish to be helped and to lean on a strong helper.

This polarity of the mental life, which can be compared with the law of action and reaction in physics, is by no means the only dynamic principle expressed in emotional syllogisms.

In the investigation of psychogenic organic disturbances, it has proved of great value to study psychic processes according to their general dynamic direction (vector quality), while ignoring temporarily the manifold variety of their ideational content. Alexander finds that the three fundamental categories of psychologic tendencies are those of intaking, eliminating and retaining. These three main classes express fundamental urges of the person, and they themselves can be subclassified into more complex tendencies, which express not only the direction of the tendency but a certain attitude of love or hate toward external objects. Thus, indulgence in the receptive tendencies often leads to the compensatory tendency to give.

In studying the dynamic relationships, the principle of polarity is striking. For example, extreme retentive tendencies increase the sense of obligation to give. The recognition that, in addition to the psychologic content, one might also understand the fundamental direction of the emotional drive lies in the fact that certain general formulas can be applied to a great many different psychologic pictures. This has been brought out by Alexander in his study of the psychologic factors in gastro-intestinal disturbances.

Alexander looks on the organ neuroses as the outcome of a disturbance of balance between the psychologic tendencies of intaking, retaining and eliminating. He believes that in the normal person a certain proportion exists between these various drives and that the proportions are different in men and women, as well as in children and adults. Disturbance of any one of these tendencies causes a disturbance in other tendencies, with the whole organism becoming involved.

KASANIN, Chicago.

**PURPOSIVE ACCIDENTS AS AN EXPRESSION OF SELF-DESTRUCTIVE TENDENCIES.**  
KARL A. MENNINGER, Internat. J. Psycho-Analysis 17:6 (Jan.) 1936.

A discussion of accidents which on analysis appear to be unconsciously purposive is undertaken by Menninger as further evidence of the motives and devices of self-destruction. Five clippings from the press illustrate cases of persons who have either killed or wounded themselves by walking into burglar traps of their own design. Examples of automobile accidents and other types of accidents occurring during a period of psychoanalysis and hence subject to psychologic examination are also reported. It is impossible to do more than infer the purpose of accidents reported in the press, but in cases in which there is psychoanalysis, one can see how the accident serves to punish the subject for guilty acts or wishes and at the same time, when the outcome is not fatal, to permit further indulgences in the same guilty acts or fantasies. The local self-mutilation appears to be a ransom which protects the ego against the imposition of the death penalty. "Hard luck champions," whose lives are a series of mishaps, are also mentioned. One of the author's patients had had twenty-four major disasters in his life, including the accidental poisoning of his own child, and eleven automobile accidents. His guilt arose in part from terrific but unconscious wishes to kill certain members of his family. The same motives pointed out by Menninger in other forms of self-destruction are described as determining these purposive accidents, e. g., elements of aggression, punition and propitiation, with death as the occasional but exceptional outcome.

KASANIN, Chicago.

## AUDIOMETRIC EXAMINATION OF PATIENTS WITH VERBAL AUDITORY HALLUCINATIONS. FERDINAND MOREL, Ann. méd.-psychol. 94:520 (April) 1936.

Morel reports the results of auditometric examination of thirty-one patients, most of whom had had chronic auditory hallucinosis for from a few months to several years; others had dementia praecox and subacute alcoholic psychosis with verbal hallucinations. He found that in cases of chronic hallucinosis, even of long standing, there occurs no change in the acuity of hearing and no auditory scotomas are observed. So long as the external or the internal ear is not diseased, the audiograms of patients taken when they are not hallucinating do not differ from those of normal persons. On the other hand, disease of the ear affecting the acuity of hearing does not alter the character or content of verbal auditory hallucinations. Audiograms taken at the time when patients had auditory verbal hallucinations (hearing of "voices") revealed several interesting abnormalities. First, there occurred immediately a rise of the threshold of hearing, with resulting momentary cleavage between the normal threshold of the patient and the threshold obtained at the time of the hallucinations. The duration of the phenomenon is a few fractions of a second; it may occur during the audiometric test as a series of paroxysmal elevations of the threshold of hearing. Morel compares the effect of the hallucination on auditory acuity to intermittent claudication of hearing. The momentary rise of the threshold of hearing coincident with auditory hallucinations is shown on the audiogram by an irregular "fringe" of threshold points above the curve for the normal threshold of hearing of the patient. The record of the latter for a given patient is always the same, while the "fringe" is extremely variable from one examination to another; the "fringe" may be present on one day and absent on another; it may appear at one time over the sector of low pitch (low frequency), and at another time it may shift and appear over the sector of high pitch (high frequency). It appears as though there occurs between the sound stimulus and the false perception a sort of contest in which the latter always wins and alone is listened to by the patient, without, however, total loss of objective hearing. Thus, one patient stated that when the sound of the audiometer and the "voices" occur simultaneously, "the voice is the stronger," "the voice is on top" (*la voix couvre*); another stated that "one cannot pay attention to both at the same time"; another claimed that "when voices come at the same time as the musical sound" he gave "preference to the voices." In this patient the difference between the normal threshold of hearing and the "fringe" was at times as great as 45 decibels. When patients were requested to compare the "voices" with the audiometric sounds of varying pitch and intensity, they were not able to do so. In this feature the auditory hallucinations differ from the so-called "entotic sounds" (subjective whistling, ringing and humming sounds of otogenic origin). The latest-mentioned "sounds" often were identified by the patients with the audiometric sounds of definite pitch and intensity. Furthermore, the auditory hallucinations were never associated with lowering of the threshold of hearing, i. e., with an increase of auditory acuity, while the "entotic sounds" often were. Morel cites the case of a patient who, besides verbal hallucinations, had rhythmic "entotic sounds" (something like a short whistle) occurring at regular intervals. The audiogram of this patient showed, besides the usual "fringe" of hallucinatory threshold superimposed, on the normal threshold of hearing, threshold points below that of her normal hearing acuity coincident with "entotic sounds." This shows that the mechanisms of verbal auditory hallucinations and of the "entotic sounds" are different. The verbal hallucination is an essentially negative phenomenon, a hole or temporary anesthesia in the elementary hearing. It may be regarded as a temporary impediment of auditory function occurring during the perception of elementary periodic sound. However, this impediment in the function of elementary hearing is probably only one aspect of the impediment of more elaborate auditory functions, such as hearing and comprehension of spoken words. Morel has observed that a verbal hallucination may be associated with momentary word deafness and that in some instances the patients were momentarily unable to recognize and identify familiar sounds. In other words, in these instances there was not only word deafness but actual cortical deafness—auditory agnosia. The abstract does not cover all the important points of this article.

YAKOVLEV, Waltham, Mass.

THE ACQUIRED DEMENTIAS. ERNST GRÜNTHAL, Fortschr. d. Neurol., Psychiat.

7:241 (June) 1935.

Grünthal presents a review of clinical and histologic reports that have accumulated during the last three years in cases of presenile psychosis and senile dementia. Of the ten cases of Pick's disease mentioned, two were of unusual interest in that well developed symptoms of extrapyramidal involvement were noted. Histologically, cortical atrophy with diminution in the size of the substantia nigra and caudate nucleus was found. In a case of Van Husen's, although clinically not unusual, there was histologic evidence of shrinkage in the anterior portion of the central convolution. Further evidence that histopathologic changes may occur in various areas of the brain in this disease is offered by the case of Lhermitte and Trelles. In this instance the disintegration of higher motor activities was most prominent. On histologic examination a bilateral, symmetrical, circumscribed cortical atrophy was noted which extended from the anterior portion of the inferior parietal gyrus to the supramarginal and the angular gyrus. A similarly circumscribed lesion was found in a case described by Frets in which there were amnesia, aphasia and symptoms of dementia.

To support the contention that Pick's disease may be hereditary, Grünthal offers four illustrative cases. Outstanding is one reported by Schmitz and Meyer, in which atrophy of the frontal lobes and clinical symptoms of marked emotional indifference and lack of initiative were presented. Slight cellular changes were observed in the corpus striatum, the pallidum and the substantia nigra. The father and two sisters of this patient were afflicted in similar manner; also the father's brother and his son. A nephew of the uncle, whose parents were said to have been well, was considered to have a psychopathic personality. Grünthal discredits Mayano's attempts to contest the hereditary factor in Pick's disease on the basis that the material studied by Mayano was to a great extent more suggestive of Alzheimer's than of Pick's disease. Theoretical speculations made by Korbsch, Onari and Spatz that superficial anatomic similarities in Huntington's chorea and Pick's disease might involve also an etiologic relationship between these two diseases are considered as unacceptable by the reviewer.

In the last three years Schottky has reported nine cases of Alzheimer's disease, in six of which the anatomic observations substantiated the diagnosis. Grünthal comments on seven new cases. Alzheimer's disease in association with disturbances of the endocrine system has been noted on three occasions: once with Simmond's hypophysial cachexia and twice in association with myxedema. At present there seems little evidence to ascribe a causal relationship between the two diseases mentioned, nor can a common underlying factor be found. Fenyes and Hallervorden have shown conclusively that the intracellular neurofibril changes so characteristic of Alzheimer's disease have been found in the brain stem in nearly every instance of Economo's disease in its advanced stage. It would seem that these particular histologic changes need not be associated necessarily with senile conditions, and, conversely, the authors believe that Alzheimer's disease is not necessarily indicative of a presenile condition. The case reported by James appears to be the only one in which familial occurrence of this disease is at all substantiated.

The cases of Krapf are grouped together to represent a general syndrome of cerebral atrophy. Such conditions are seen in persons in the seventh and eighth decade of life. Psychic manifestations appear to differ in the cases with known arteriosclerosis and hypertension from those with arteriosclerotic changes and hypotension.

Morel has described cases of internal frontal hyperostosis with adiposity and cerebral disturbances. The changes in calcium metabolism are held responsible for the hyperostosis. The tendency to adiposity, disturbances of sleep, hyperorexia, polydipsia, muscular weakness, optical changes, headaches and late occurring epileptiform seizures have been ascribed to changes in the hypothalamus, characterized by a decrease in the number of cells. Grünthal believes, however, that the arteriosclerotic vascular changes may be responsible for many of the clinical symptoms.

Kraepelin has defined a special group among the presenile dementias in which anxiety, states of depression or excitement and simulation of organic disease processes may be found. The course of the disturbance is long in duration and may lead to severe dementia. Grünthal reports one case which in many respects is similar to the six cases described by Kraepelin. Further similarity is shown in the histopathologic picture, which consists in the main of shrinkage in the cells of the cortical layers and of liquefaction of cells, which may also be seen in the corpus striatum and the dentate nucleus.

The diagnosis of senile dementia must be made with great care, as frequently the demarcation between normal changes inherent to old age and the disease processes of this age group is not obvious. There is no correspondence between the degree of histologic change and the degree of clinically observed senile dementia. Furthermore, Gellerstedt and Friesel found that histologic changes in brains of old persons without dementia may be very similar to those in the brains of persons with senile dementia. Grünthal's work on this subject confirms the findings of Gellerstedt and Friesel.

Scheele reported on senile dementia observed in twins. The clinical course and symptoms in the twins were very similar. These two dementias were also in many respects similar to the one from which the father of the twins had suffered.

The question of heredity in senile dementia remains unsolved. Pearl and Greef in their studies on longevity believe that hereditary factors are at play. What relationship exists between longevity and the occurrence of pathologic senile changes is not determined.

RICHTER, Chicago.

FUGUE REACTION DURING THE COURSE OF A CATAPHRÉNIC EPISODE. EUGEN VON THURZÓ, Ztschr. f. d. ges. Neurol. u. Psychiat. 153:222 (July) 1935.

On Aug. 8, 1934, a Pole aged 39 was picked up in a Hungarian town because of suspicious behavior. He had had a febrile disease in 1934, after which he began to roam about the house aimlessly and apparently in a confused state. He left home twice for short periods before he wandered away on May 25, 1934. He had been roaming about for three months before he was found in Hungary. He had passed through the Carpathian mountains, crossed the borders of two countries and wandered through poorly frequented wooded lands, with bad roads. On his admission to the hospital, there were ecchymotic discolorations of the eyelids; the left elbow was swollen, with a number of blebs on the extensor surface; the movements of the elbow were limited, and the hands and feet were cyanotic and cold, with cutis marmorata of the legs. There was no disease of the internal organs.

Neurologic examination showed slight irregularity of the right pupil, which was a trifle larger than the left; the reactions of the pupils to light and in accommodation were normal; there was slight weakness of the right lower part of the face on volitional innervation; the palatal reflexes were not elicited; the right ankle jerk was not obtained; the abdominal reflexes were absent; associated movements of the forehead on looking up and of the platysma muscle during tight closing of the jaws were defective; at times the lingual-mental reflex was positive; blepharospasm was definite; there were lively pilomotor reflexes, and dermographism was intense.

Mental examination showed mutism, with a vacant, staring expression interrupted only by an occasional sigh. The facial expression was at times that of anxiety; there was no response to questions or simple commands; the patient did not imitate movements of the examiner; mild negativism was present; there was only a mild defense reaction when objects were quickly passed before his eyes; he responded only to painful stimuli; he showed little interest in his surroundings, though he ate without aid and was not untidy; sleep was undisturbed; flexibilitas cerea was noted.

This catatonic syndrome lasted three weeks. The patient improved gradually and began to talk freely about himself. The anamnestic data were checked by

information obtained from the wife. There was complete amnesia for the three months of nomadism, in spite of the fact that the patient must have done relatively complicated things to cover such a long distance and sustain himself throughout this time. He did not recall being taken into custody by the police after he reached Hungary. His behavior became normal, though he was resentful toward his wife because he felt she neglected to give him proper medical attention and injured him by the administration of home remedies. Mild hypomimia and bradykinesia persisted.

This syndrome resembling schizophrenia with a period of poriomania is, according to Thurzó, a symptom of chronic encephalitis. Onset of this disease was with a definite febrile reaction; perusal of the positive neurologic findings shows ample evidence to substantiate the theory that the patient had epidemic encephalitis. The author utilizes the term cataphrenia as it was used by Jolly for the catatoniform clinical pictures resembling schizophrenia, which have been observed occasionally to follow epidemic encephalitis. Austregesilo coined this term to designate recoverable psychoses resembling dementia praecox, usually encountered in the course of other diseases. Thurzó was unable to find a similar case in the literature, though this reaction pattern (poriomania) is not unknown in cases of epilepsy and hysteria.

SAVITSKY, New York.

### Meninges and Blood Vessels

OCULAR COMPLICATIONS OF CEREBROSPINAL MENINGITIS. E. B. DUNPHY, Arch. Ophth. 15:118 (Jan.) 1936.

This article is an ophthalmologic review of the literature on cerebrospinal meningitis, from the time it was first described, in 1805, by Vieusseaux and Matthey. The uveal tract and the retina are both involved at times. Apparently, the infecting organism is conveyed to the eye by way of the blood stream and not by direct spread from the meninges. In almost all cases the ocular inflammation begins during the stage of bacteremia, though later involvement of the eyeball may occur owing to septic emboli. Collins and Mayou examined an eye with this complication pathologically and observed an embolus lodged in the ciliary body. The organism has been demonstrated within the eyeball on several occasions. Axenfeld cultivated it from an eye post mortem. McKee demonstrated it in the anterior chamber post mortem, and Weakley aspirated pus from the anterior chamber during the development of uveitis and from it grew a pure culture of the meningococcus.

Pathologic changes in the conjunctiva have long been recognized as a complication of epidemic meningitis. McKee made careful bacteriologic studies in six cases and in two cases obtained a pure culture of the meningococcus. Occasionally the meningococcus has been noted in the eyes of patients not ill with epidemic meningitis. This led McKee to suggest that the eye might be a portal of entry for the infection. The cornea is not frequently involved. Parenchymatous keratitis has been observed. Corneal ulcers have been reported by several observers.

Pupillary abnormalities have been frequent. Dilatation and fixation of the pupils have occurred, each of which disappeared after subsidence of the infection. Inequality of the pupils has been observed. Hippus has occurred in a large number of cases, and in several instances there has been complete absence of the light reflex. Paralytic convergent strabismus has been found infrequently. Nystagmus is rare; in three of the seven instances in which it was noted it was vertical, and in one, rotary. It is a grave prognostic sign.

Optic neuritis is not infrequent, but papilledema is rare. True optic neuritis has been reported in from 4 to 18 per cent of cases, while papilledema was observed in only one instance. Three cases of retrobulbar neuritis have been reported in the literature; the patients were completely blind, without ophthalmoscopic lesions. In one of these cases autopsy was performed, but the cause of the blindness was not determined. Lewis, who discussed this, expressed the belief

that in such instances the cause must be a lesion anterior to the primary optic centers—probably intense neuritis at the chiasm. He suggested that if the blindness is cortical one would expect retention of pupillary reactions.

Complete blindness has been noted as an early manifestation in infants. It is due not so much to optic neuritis as to an overwhelming toxic impairment of the higher visual centers. In these cases the pupils remain active, though sluggish, and sight has been restored in many instances.

SPAETH, Philadelphia.

PERMEABILITY OF THE MENINGES TO ARSENIC IN CASES OF DEMENTIA PARALYTICA BEFORE AND AFTER MALARIA THERAPY. D. PAULIAN, Ann. de méd. 39:375 (April) 1936.

While in normal persons the hemato-encephalic barrier is impermeable to arsenic, it is more or less permeable in all patients with dementia paralytica. The localization of this changed permeability is probably the endothelium of the cerebral vessels, which have been damaged by the syphilitic disease. After intravenous injections of neoarsphenamine, the maximum amount of arsenic in the cerebrospinal fluid after approximately four hours was found to be from 1.8 to 4 mg. per thousand cubic centimeters. On the other hand, in the blood the amount of arsenic was markedly diminished after that period, probably owing to fixation of the arsenic by the reticulo-endothelial system. In the urine the maximum amount eliminated after half an hour was from 40 to 60 mg. per thousand cubic centimeters; four hours after injection the elimination of arsenic was diminished to from 9 to 14 mg. After malaria or vaccine therapy the permeability of the hemato-encephalic barrier was markedly diminished, probably owing to healing of the vascular lesions, as indicated by the clinical improvement. Four hours after injections of arsenic the amount of arsenic in the cerebrospinal fluid in the patients treated with malaria therapy was reduced to from 0.8 to 0.12 mg. per thousand cubic centimeters, while in the blood the amount remained about the same as before treatment (from 10 to 16 mg.). These changes in the permeability of the hemato-encephalic barrier to arsenic are a reliable indicator of the success of treatment, for in cases in which clinical improvement is not shown, the amount of arsenic in the cerebrospinal fluid was not diminished.

WEIL, Chicago.

MULTIPLE ORBITOCRANIAL LESIONS FROM A LEAD SHOT: SYNDROME OF HEMORRHAGE OF THE CAVERNOUS SINUS. C. DEJEAN, Rev. d'oto-neuro-opht. 13: 782 (Dec.) 1935.

Hemorrhage from the cavernous sinus has rarely been observed; usually it has been the result of a penetrating wound through the orbit or a complication of fracture of the vault of the orbit or the base of the skull.

The case reported was that of a man aged 37 who received in the left side of the face and neck a charge of shot fired from a distance of 40 meters. Profuse hemorrhage (estimated at 2 liters) occurred from the eye and nose but ceased eventually. Examination revealed wounds of the face and neck and a single small wound of the eyelid and globe 5 mm. outside the corneoscleral junction, at the meridian of 4 o'clock. Vision in the left eye was reduced to perception of light. There was ptosis of the right eyelid, and all muscles supplied by the right third nerve were paralyzed. Roentgenograms localized the shot in the right temporal fossa, a short distance from the squama. Two days later hemiplegia occurred on the left side; it disappeared after about three weeks, but paralysis of the oculomotor nerve persisted for several months. Atrophy and loss of vision eventually occurred in the left eye. The track of the shot was almost horizontal and oblique from before backward and from left to right; it involved the left eye, the posterior portion of the ethmoid labyrinth, the body of the sphenoid bone and the middle fossa and must have included the cavernous sinus. The right oculomotor nerve was injured by the shot, a spicule of bone or the effusion of blood. The

hemiplegia was attributed to the spread of blood along the base of the skull, thus compressing the peduncle, although it may have been due to spasm of a large artery.

Wounds of the cavernous sinus are characterized by profuse external and intracranial hemorrhage, followed by spontaneous arrest if the wound is not too large, and encephalic compression from hematoma, which may involve the second, third, fourth, fifth and sixth nerves.

DENNIS, San Diego, Calif.

**TUMOR SYNDROME WITH HYPERTHERMIA AND VISCERAL DISORDERS DUE TO CHRONIC BASILAR TUBERCULOUS MENINGO-ENCEPHALITIS.** P. MARTIN and L. VAN BOGAERT, *J. belge de neurol. et de psychiat.* **35:**767 (Dec.) 1935.

A woman aged 32 first noticed migrainous headaches accompanied by vomiting at the onset of each menstrual period. Examination revealed moderate gastric retention with dilatation of the duodenum. Gastro-enterostomy relieved the symptoms only temporarily. The headaches became more severe, and two years later the patient experienced attacks of hyperthermia accompanied by vomiting. There were intense and persistent epigastric pain and marked rigidity of the neck. Examination of the spinal fluid gave negative results, and ventriculography showed only a moderate internal hydrocephalus. Tumor of the third or fourth ventricle was suspected.

Postmortem examination revealed the presence of a localized area of tuberculous meningo-encephalitis, involving principally the region of the optic chiasm, the diencephalon, the infundibulum and the mamillary bodies. The authors explain the symptoms, principally the hyperpyrexia and the visceral symptoms, as due to involvement of the hypothalamic nuclei and make the statement that many visceral difficulties the pathogenesis of which remains obscure may be due to lesions or functional disorders of the hypothalamus.

WAGGONER, Ann Arbor, Mich.

### Diseases of the Brain

**THE POSSIBILITY OF PURE MOTOR APHASIA.** J. M. NIELSEN, *Bull. Los Angeles Neurol. Soc.* **1:11** (March) 1936.

Nielsen reports the case of a man aged 28 who had been struck by an automobile three days before his admission to the hospital. On regaining consciousness he walked to the sheriff's office, where he talked with difficulty and appeared disoriented. Two hours later he was totally unable to speak. Neurologic examination revealed no abnormalities except aphasia. The patient was alert, attentive and cooperative. He was unable to pronounce a word but made gutteral sounds. He could not write with the right hand, apparently because of pain, but could write spontaneously and to dictation with the left. He executed complicated spoken commands expeditiously and accurately. He read correctly and seemed to recognize and use correctly objects around him. The only sign of apraxia was inability to whistle. Mental calculation was accurate and rapid. The author calls this a picture of "subcortical motor aphasia," which he attributes to a disturbance in the white matter below Broca's convolution.

MACKAY, Chicago.

**EXTREME ENCEPHALITIC PARKINSONISM WITH CONTRACTURES WHICH RELAX DURING SOMNAMBULISTIC STATE.** J. M. NIELSEN, *Bull. Los Angeles Neurol. Soc.* **1:28** (March) 1936.

Nielsen reports the case of a boy aged 16 years who began at the age of 10 years to have tremors and rigidity, first on the right side and then on the left. Gradually the whole body became stiff, with flexion contractures, until he was permanently confined to bed and was unable to turn over. His speech became

lalling and unintelligible. Under slight emotion he exhibited exaggerated laughing or crying. Under emotional stress he was sometimes seen to extend his supposedly contracted arms and hands. One year before examination his father saw him jump out of bed and walk "with complete absence of contracture," in a somnambulistic state. Examination revealed universal rigidity in flexion. The limbs could not be extended passively. There were masked facies, cogwheel movement, increase in tendon reflexes and absence of abdominal and cremasteric reflexes. No pathologic reflexes were elicited. There was profuse sweating. The diagnosis was chronic encephalitis with parkinsonism.

MACKAY, Chicago.

TRAUMATIC EPILEPSY. C. P. SYMONDS, *Lancet* 2:1217 (Nov. 30) 1935.

Symonds summarizes the causes of traumatic epilepsy as follows: In association with penetrating injury it is due to infection of the meninges and brain; in a small number of cases in which the fits occur within a few hours or days of the injury, epidural subdural or subarachnoid hemorrhage is the usual cause, and in the great majority of cases the cause is direct injury to the brain substance occurring at the moment of injury, with subsequent cicatricial change. For this study Symonds has chosen twenty-eight cases in which the injury occurred in civil life and was of the "closed" variety. There was an average latent period of two years and nine months between the injury and the attacks. In seventeen cases the interval was from three months to eighteen months. In the remaining nine cases the range of the interval was from two to sixteen years. Generalized attacks occurred in twenty-four instances, generalized attacks with a focal aura in two and Jacksonian attacks in two.

It is Symonds' opinion that, once established, the attacks tend to persist and usually become more frequent and severe. The medical treatment of traumatic epilepsy differs in no wise from that of idiopathic epilepsy. As for surgical treatment, he refers to the work of Foerster and Penfield, who advocated excision of the cicatrix, when this can be localized either from the focal nature of the attacks or from the evidence obtained by injection of air into the ventricular system.

From an analysis of his own cases and those of other authors, Symonds finds that the incidence of epilepsy is higher in the group of patients with fracture of the skull, especially fracture of the vault. He asks: "Are we going to accept the very fact of past injury to the head as evidence of a traumatic cause for the epilepsy, provided that no other cause can be found and the family history is negative?" His answer is "no." He states that the history must be that of an adequate injury to the head. He lays stress on symptoms such as headache, insomnia, difficulty in concentration and giddiness persisting for months after the injury, though not necessarily up to the time of the first fit. Also, the presence of blood in the cerebrospinal fluid shortly after injury strongly indicates the probability of cortical laceration.

Of the patients with traumatic epilepsy in this series whose cases involved compensation, 75 per cent had accepted final settlements before the first fit occurred. Subsequently they were disabled, without hope of further recompense. Under the Workmen's Compensation Act in England, there is a provision whereby the injured person may accept the settlement of a lump sum on condition that if a specified complication should arise later, the question of compensation may be reopened. In Symonds' opinion, this provision should be utilized against the risk of traumatic epilepsy much more often than it is at present.

WATTS, Washington, D. C.

AUDITORY HALLUCINATIONS IN A CASE OF ASTROCYTOMA OF THE LEFT TEMPORAL LOBE. EGAS MONIZ and ROMAO LOFF, *Encéphale* 30:20 (Jan.) 1935.

Moniz and Loff, after discussing the rarity of auditory hallucinations in association with cerebral tumor, report the case of a woman who at the age of 37 began to have attacks of altered consciousness, beginning with a sense of constriction

passing from the epigastrium to the external genitalia and hearing the voices of unknown persons. There were no convulsions. Four and one-half years later she began to have severe headaches, nausea, vomiting and visual disturbances. Examination revealed papillary stasis, paralysis of the left oculomotor nerve and right hemiparesis and hyperreflexia, with a negative Babinski reaction. There were mental torpor and slightly diminished hearing on the left.

Arteriography and phlebography aided in establishing the diagnosis of tumor of the left temporal lobe, which was confirmed at operation. Necropsy revealed that the tumor, an astrocytoma, lay in the middle portion of the first two left temporal convolutions, invaded the insula, the claustrum, the putamen and the internal capsule and compressed the left cerebral peduncle. The authors conclude, after a brief discussion of the auditory centers, that tumor of the middle portion of the temporal lobe may give rise to verbal auditory hallucinations.

MACKAY, Chicago.

ENCEPHALITIS OF THE BRAIN STEM ASSOCIATED WITH GONOCOCCIC DISEASE.  
OTTO SITTIG and VLADIMIR HASKOVEC, *Encéphale* **31**:159, 1936.

A man aged 25, with gonorrhreal urethritis four days after exposure, noted pains in the eyelids and insomnia seventeen days after the onset of urethritis, followed by vertigo, clouding of vision, unsteadiness of gait and a nasal voice. Examination showed dilatation of the pupils, which reacted feebly to light, restriction of movements of the eyeballs in all directions, nystagmus, paralysis of the palate, abolition of all deep reflexes of the extremities, a Romberg sign, ataxic gait and ataxia of the upper limbs. The urethral pus contained the gonococci. The reaction to the complement fixation test was positive for the blood and negative for the spinal fluid, which was normal. Reactions to serologic tests for syphilis in blood and spinal fluid were negative. The eyegrounds were normal. Three days later the movements of the eyeballs were practically absent in all directions. In the course of two months the signs and symptoms gradually disappeared, leaving only nystagmus in the extreme lateral position of the eyeballs. At no time were there fever, somnolence, mental disturbances or symptoms of involvement of the joints or heart. The general condition remained good throughout. Treatment consisted of methenamine, administered by mouth and by urethral injections. When the patient left the hospital, he was free from urethral discharge, and no gonococci were observed.

The clinical picture resembles that of Wernicke's superior hemorrhagic polioencephalitis but differs from it in the absence of mental disturbances and somnolence and in its relative benignity. Reports of various nerve complications of gonorrhea, mostly neuritis and meningitis and sometimes myelitis and focal cerebral lesions due to embolism from gonococcic endocarditis, were found in the literature.

LIBER, New York.

ANATOMIC PROBLEM OF PALATAL MYOCLONUS. P. HILLEMAND, J. A. CHAVANY and O. TRELLES, *Rev. neurol.* **64**:1 (July) 1935.

The authors restudied the four cases reported by Foix in which palatal myoclonus was associated with infarcts in the tegmentum of the pons, destroying the central longitudinal fasciculus, and with hypertrophic degeneration of the olfactory body. They found in the literature seven other cases of the same type. They made a second group of cases in which there existed a lesion of the dentate nucleus and of the contralateral olfactory body, with integrity of the central tegmental fasciculus. They report also a single observation in which there was a pure degenerative lesion of the olive, with integrity of the central tegmental fasciculus but involvement of the olivodentate fibers and secondary degeneration of the dentate nuclei. This case was reported by Guillain, Mollaret and Bertrand, in 1933.

The central tegmental fasciculus is an important tract, particularly in the upper part of the pons. It connects the thalamus and the hypothalamic nuclei, especially the red nucleus, with the medullary olive, and it has important connections with the cerebellum. In cases in which a lesion involves the red nucleus and its capsule, there are degeneration of the central tegmental fasciculus and pallor of the periolivary stratum on the same side. Moreover, there is apparently a transsynaptic degeneration affecting the olivocerebellar fibers. However, as Lhermitte has shown, there are exceptions to this, since hypertrophic degeneration of the olive may take place without degeneration of the central tegmental fasciculus, and vice versa.

Recent investigators have described both direct and crossed fibers entering the central tegmental fasciculus from the striate body. From the physiologic standpoint the central tegmental fasciculus seems to play an important rôle in fasciorespiratory synkinesis. While most cases can be satisfactorily explained on the basis of a lesion of the central tegmental fasciculus, the theory fails to the ground on account of the presence of palatal myoclonus in cases of degeneration of the dentate nucleus. The dentate nucleus is apparently closely bound to the olfactory body, and in certain cases of the syndrome of myoclonus and epilepsy fatty degeneration is observed in the dentate nucleus and the olfactory body. However, there are numerous cases in which softening of the dentate nucleus is not associated with palatal myoclonus. Moreover, myoclonus appears not after destruction of the fibers running between the dentate nucleus and the olive but apparently only with destruction at their source or termination. In all cases of palatal myoclonus the olfactory body of the opposite side appears to be affected. This seems to be the outstanding feature. Whether this occurs in response to degeneration in the central tegmental tract or the olivodentate fibers or to a peculiar degeneration that appears to be connected with obliteration of the small arteries running to the olfactory body itself, the authors insist that the olive must be degenerated before myoclonus can occur.

FREEMAN, Washington, D. C.

RELATIONS BETWEEN THE COCHLEOVESTIBULAR SYSTEM AND THE OCULOMOTOR SYSTEM IN A CASE OF POSTTRAUMATIC PARALYSIS OF THE OCULAR MUSCLES.  
V. TANTURRI, Rev. d'oto-neuro-opht. 13:509 (July-Aug.) 1935.

After an accident, in which his head was crushed between two motor vehicles, Tanturri's patient complained of head noises, vague vertigo and diplopia. Examination revealed complex disturbances of the ocular movements of both eyes consisting of paralysis of both external rectus muscles and of upward and downward movements of the globe. In fixing on an object which was slowly displaced laterally, the eyes turned beyond the limit of the paralysis. There were in addition, spontaneous irregular nystagmus toward both sides; bilateral hypo-acousis, with reduced bone conduction and concentric limitation of the auditory fields; minimal reactions to stimulation of the labyrinth; diminished nystagmic reaction after turning; marked hypo-excitability in the caloric test, and normal reactions to the galvanic test.

The ocular paralytic syndrome may be localized with probability in the corpora quadrigemina. The puzzling question is whether the cochlear and labyrinthine phenomena are the result of peripheral or of central lesions. The ocular movements provoked by the fixation of an object which is moved slowly and reflex labyrinthine movements are of different nature. The preservation of provoked nystagmus in a case of paralysis of the ocular muscles does not mean certainly the existence of a supranuclear lesion, for in a case previously observed the cortical oculogyrical stimulations were active and intervened to stop the nystagmus produced by labyrinthine stimulation. When reflex vestibular movements of the eyes are conserved and voluntary movements are lacking, it is logical to assume that the lesions of the oculogyrical pathways are supramesencephalic. In the case cited, it was believed that the lesions were located in the posterior longitudinal bundle and that the indirect pathways traversing the reticulated system were intact. The validity of the belief of a number of writers that strabismus is of

labyrinthine origin is placed in doubt by the investigations of Sommer and Tanturri. A number of observers have reported cases of ocular paralysis due to a lesion in the pons, and it is known that in animals interruption of the posterior longitudinal bundle causes ocular paralytic phenomena. Spiegel assumed that the vestibulo-ocular tract represents a common pathway for both cortical and vestibular ocular movements. Bárány's assumption of a supranuclear center for the quick phase of nystagmus, located around the aqueduct and in the reticular formation, is not confirmed. According to Brunner, the lesions that abolish nystagmus are destruction of the ocular nuclei, destruction of the posterior longitudinal bundles and destruction of the longitudinal bundle of one side and a lesion of the bundle on the other.

The complexity and bilaterality of the ophthalmoplegia in the case reported exclude a simple lesion of the tip of the petrous process; the paralysis must be explained by a nuclear lesion. In lesions of the quadrigeminal bodies, difference in the size of the pupils has been observed, and Spiegel postulated a nucleus for pupillary accommodation to light, situated around the aqueduct. If the lesion extends downward toward the locus caeruleus or the medullary velum, disturbances of mastication, due to a lesion of the nucleus of the fifth nerve, are observed. The hypothesis that the vestibular lesions are peripheral cannot be excluded, because of: (1) dissociation in the labyrinthine tests; (2) the fact that hypo-excitability is usually observed after a peripheral lesion; (3) concomitance of cochlear phenomena, and (4) the fact that vestibular symptoms are rarely observed in lesions of the corpora quadrigemina. On the other hand, there were complete absence of concomitant general phenomena (rotary vertigo and falling) and deviation to the left in walking (i. e., toward the side of the quick phase of nystagmus); both phenomena point to a central lesion. The question whether the cochlear impairment was peripheral or central in origin is discussed pro and con. Tanturri believes that after the traumatism small hemorrhages were formed at the level of the posterior corpora quadrigemina, which explains the ocular paralysis, that the cochlear and vestibular disturbances are due to either central or peripheral lesions and that, from a clinical point of view, the topographic diagnosis of these alterations is extremely difficult.

DENNIS, San Diego, Calif.

**UNILATERAL GLOBAL PARALYTIC SYNDROME OF THE TWELVE CRANIAL NERVES.**  
H. ROGER, C. ROCHE, N. CARREGA and J. PAILLAS, Rev. d'oto-neuro-opht.  
**14:241** (April) 1936.

The authors describe in detail a new case of unilateral global paralysis of the cranial nerves, due to extension to the base of the skull of an epithelioma of the nasopharynx. In brief, the patient, who had a latent epithelioma of the cavum, first presented a cancerous tumor of the neck, the origin of which was not discovered until seven months later. After six months progressive paralysis of the cranial nerves appeared on the left side, beginning with facial neuralgia and ocular paralyses. Roentgenotherapy did not retard the rapid progress and fatal termination of the disease. Characteristic of this syndrome are clinical onset with facial neuralgia, metastatic adenopathy and absence of early evidences of the primary rhinopharyngeal growth. Multiple roentgenograms of the skull, taken in various positions, are often of great aid in the diagnosis, by furnishing evidence of destruction of bone by the tumor. The relatively slow evolution of the tumor, considering the importance of the osseous destruction, is accounted for by the resistance of the meningeal barrier.

DENNIS, San Diego, Calif.

**APPEARANCE OF SPASMODIC LAUGHING IN TWO CASES OF DISSEMINATED SCLEROSIS.**  
V. DIMITRI, Arch. argent. de neurol. **13:3** (July-Aug.) 1935.

Dimitri reports two cases of disseminated sclerosis with spasmodic laughing, in both of which lesions in focal areas of the brain were shown at autopsy. In

one case this symptom developed early in the disease, but in the majority of instances it appears when the disease is advanced. There is no relation between the laughter and the emotions. Sometimes the laughter is explosive and at other times mild. In cases of spasmodic laughter there is none of the mobility of facial expression seen in the normal person; rather, the laughter is carried out with more or less rigid facies. The laughter is usually initiated by some humorous thought or act. There has been much diversity of opinion concerning the pathogenesis of spasmodic laughter and crying. Some have attributed it to involvement of the lower bulbar centers (Oppenheim); others (Wilson and Brissaud) expressed the belief that pathologic laughter and crying can be initiated by purely pyramidal lesions. Wilson stated that there is in the pyramidal tract a pathway which regulates involuntary or emotional expressions. These pathways, which unite the cortex with lower centers, pass by the thalamus, to enter the subthalamic region. Others claimed that the striatum is responsible for such automatic acts as laughing and crying. Bechterew placed the centers of expression in the thalamus, attributing involuntary emotional expressions to lesions in this nucleus. Jakob made a study of pseudobulbar palsy with spasmodic laughter and observed lesions of the thalamus in only two cases. In most of his cases he observed no lesions of the thalamus, so that he looked on spasmodic laughter as due not to a focal lesion in the thalamus but to lesions in the anterior portions of the frontal lobe existing conjointly with thalamic disease.

In the two cases reported by Dimitri there were lesions in the thalamus involving chiefly the medial nuclei but also the lateral nucleus, the center median nucleus of Luys and the pulvinar. There were also lesions in the lenticular nucleus, especially in the pallidum. The cerebral hemispheres were little involved in one case and not at all in the others. Dimitri places great importance on the constant lesions in the thalamus. He points out that the medial nucleus of the thalamus receives fibers from the frontal cortex, by way of the anterior limb of the capsule. By means of this there is inhibition of the cortical centers in automatic acts. Consequently a lesion in the thalamus would be responsible for involuntary laughing and crying.

ALPERS, Philadelphia.

HEREDITARY FACTOR IN EPILEPSY. KLAUS CONRAD, Ztschr. f. d. ges. Neurol. u. Psychiat. 153:271 (July) 1935.

Conrad presents evidence to support the hypothesis that there is a significant hereditary factor in epilepsy. He obtained definite information regarding the existence or nonexistence of twins in 12,561 epileptic patients who were patients in various German institutions on Feb. 1, 1934. This cross-sectional method of studying the problem was preferred to that of collecting material over a long period. It avoids a number of errors, such as counting the same patient twice, difficulty in finding relatives and inaccuracy of records. There were 258 pairs of twins in which one of the pair suffered from epilepsy. The incidence of twin birth among epileptic patients was 1:48.6, as compared with 1:60.6 for the population of Germany, according to the official statistics of 1932. Dissimilar twins among epileptic patients were more frequent than identical twins (175:83). The increased incidence of dissimilar twins among epileptic patients favors polyovulation as the probable cause of twins. Conrad concludes that the mothers of epileptic patients show a tendency to polyovulation. He also notes the relatively increased incidence of dissimilar twins in the children of siblings of epileptic twins. He concludes that there is some type of correlation between polyovulation and the epileptic anlage, though he is not precise regarding the nature of the relation.

The epileptic twin was not predominantly the first-born child. In fact, in families of up to 4 siblings, the epileptic twin was usually the last child. The epileptic twin was not necessarily the first child of the pair to be born. These

facts are strong arguments against the theory that birth trauma has much to do with the cause of epilepsy.

Epilepsy was found in the second twin in 3.15 per cent of dissimilar and in 6.66 per cent of identical twins. If idiopathic epilepsy alone is considered, the percentage of incidence in the second twin rises to 86 per cent for similar twins and falls to 12.5 per cent for dissimilar twins. These facts undoubtedly point to the probability that a significant hereditary factor exists in epilepsy.

There was no case of similar twins in which epilepsy was found in one twin and mental deficiency in the other. Mental deficiency occurred with four and one-half times the expected frequency among the siblings of twins. There is some correlation genetically, therefore, between mental deficiency and epilepsy, though not that of genotypic identity. With Luxenburger's method it was found that in 96 per cent of cases in which the anlage to idiopathic epilepsy existed attacks actually developed. While endogenous influences may play a rôle, hereditary predisposition is an important factor. Conrad believes that the genetic factor is important in the pathogenesis of epilepsy and that his investigation settles this controversial problem.

SAVITSKY, New York.

### Cerebrospinal Fluid

EFFECT OF ERGOTAMINE TARTRATE ON PRESSURE OF CEREBROSPINAL FLUID AND BLOOD DURING MIGRAINE HEADACHE. J. L. POOL, T. J. C. VON STORCH and WILLIAM G. LENNOX, Arch. Int. Med. 57:32 (Jan.) 1936.

To determine the physiologic reason for the dramatic effectiveness of ergotamine tartrate (gynergen) in relieving migrainous headache, the authors analyzed the effect on the pressure of the cerebrospinal fluid and the blood of the injection of the drug into eleven sufferers from migraine and into twelve normal persons. A further control was effected by injecting sterile physiologic solution of sodium chloride into four normal subjects. All injections were made intravenously. The dose of ergotamine tartrate varied from 0.12 to 0.5 mg., with an average of 0.38 mg. The headache was completely relieved by the treatment in nine of the eleven victims of migraine. The average spinal fluid pressure before injection was 113 mm. for the group with migraine and 130 mm. for the group of normal subjects used as a control. The effect of the injection was to raise the spinal fluid pressure in almost every case. The pain of the injection probably accounted for some of this rise, since an elevation was noted among the patients used as controls who received the saline solution. However, a more prolonged secondary rise was characteristic of those who received the ergotamine tartrate and amounted to an average increase in the spinal fluid pressure of about 11 per cent. The systolic blood pressure also increased to about the same degree. The pulse rate decreased an average of 13 beats per minute after the introduction of the drug.

If the migrainous headache is due to the spasm of cerebral vessels, the good effect of ergotamine could be ascribed to its tendency to improve circulation, wash away toxins and increase the oxidation of cerebral tissues. But the observations do not indicate any consistent abnormality of cerebral blood flow, so that the experiment must be considered inconclusive. The fact that the average cerebrospinal fluid pressure was lower during a migrainous headache than at other times lends support to a vascular hypothesis, but the fact that there was no chronological relationship between relief from the symptom and rise of the spinal fluid pressure casts doubt on this explanation. Furthermore, the initial cerebrospinal fluid pressure of migrainous patients cannot be considered abnormally low, even though its average is somewhat lower than that found among the small group of persons used as controls. The authors also doubt that ergotamine tartrate has a simple sedative effect on the sensory nerves, since this could not account for the effectiveness of the drug in relieving the scotomas, hemianopias and other associated symptoms of migraine.

DAVIDSON, Newark, N. J.

NEW RESEARCHES ON FORMIC ACID IN THE CEREBROSPINAL FLUID. J. HAMEL, R. BUISSON and M. CHAVAROT, Ann. méd.-psychol. **89**: 28, 1931.

In 1934 Toye demonstrated the presence of formic acid in the cerebrospinal fluid in over 50 per cent of cases of dementia praecox. Hamel, Buisson and Chavarot undertook to repeat this work, using the method of Toye and Jaulmes. They examined the spinal fluid of forty-four patients, twenty-eight of whom had dementia praecox and sixteen other mental diseases. Formic acid appeared in the spinal fluid in 75 per cent (twenty-one patients) of the group with dementia praecox and was absent in 62.5 per cent (ten patients) of the group which did not have dementia praecox.

YAKOVLEV, Waltham, Mass.

SUPPLEMENTARY REPORT ON THE BIOLOGIC PROPERTIES OF THE SPINAL FLUID IN SCHIZOPHRENIA. E. GAMPER and A. KRAL, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:258 (July) 1935.

Gamper and Kral previously showed that the spinal fluid of persons with schizophrenia causes severe inflammatory changes when injected into the anterior chamber of the eye of the rabbit and the subarachnoid space of the young white mouse. Studies made as a control with spinal fluid from patients with other psychoses and with organic diseases of the nervous system did not reveal a similar toxicity. Such findings confirmed the theory that schizophrenia is an organic disease of the brain.

The present study was made to obtain more controls and to check the previous results. In the new series the spinal fluids of sixty-three patients were investigated. A number of subcutaneous injections of the spinal fluid were given to white mice during a period of forty-eight hours. The animals were watched for three weeks. Three or four white mice were used for tests with each spinal fluid. Seven patients in this series had schizophrenia. Five of twenty mice (25 per cent) which received injections died within three weeks; two of seventy-seven mice (2.6 per cent) which received injections of the spinal fluid from the twenty-eight patients with functional psychoses succumbed within the period of observation; nineteen of eighty-five mice (22.4 per cent) which received injections of the fluid from twenty-eight patients with organic disease of the nervous system died. These investigations therefore corroborate the previous studies which indicated that the spinal fluid of patients with schizophrenia is more toxic than that of persons used as controls. The fluid from patients with hebephrenia and catatonia was more toxic than that from paranoid patients, and fluid from patients with acute forms more than fluid from patients with chronic variants. These studies suggest an organic basis for the schizophrenic process and should orient future investigators in further efforts to throw light on this baffling problem.

SAVITSKY, New York.

SUGAR IN THE BLOOD AND THE SPINAL FLUID. HEINZ BOETERS, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:462 (Jan.) 1936.

The Hagedorn-Jensen method of quantitative estimation of sugar in the spinal fluid is the most reliable. The spinal fluid should be examined as soon as possible after it is drawn. Readings for the blood and the spinal fluid should be taken at the same time. Boeters reports 986 simultaneous determinations of the sugar content of the blood and the spinal fluid. The material is large enough to be statistically reliable. The reliability of the Hagedorn-Jensen method was shown by study of the difference of two separate quantitative determinations of sugar in the same specimens of spinal fluid and of blood. The average difference in 926 such double determinations of blood was 3 mg., and in 761 studies of the spinal fluid, 1 mg.

A so-called normal series of 285 cases were studied. They represented various functional diseases of the nervous system. The average reading for the blood sugar was 98.7 mg. per hundred cubic centimeters, ranging from 75 to

125 mg. The average reading for the sugar content of the spinal fluid was 63.2 mg., ranging from 45 to 75 mg. These results do not agree with those of some investigators, who found a wider variation in the sugar content of normal spinal fluid. The ratio of the sugar in the spinal fluid to that in the blood is about 2:3, the sugar content of the spinal fluid in this series being 65.15 per cent of that of the blood.

Two hundred and twelve cases of dementia paralytica were studied. The average amount of sugar in the spinal fluid was 53.4 mg., as compared with normal figures for the blood sugar. The median of the ratio of the sugar of the spinal fluid to that of the blood was 55, as compared with the median for the "normal" series, of 63.2 per cent. The sugar level of the spinal fluid is lower in the earlier stages, in which the patients present themselves for the first time for treatment—50.1 mg. in 45 cases. An absolute and relative diminution of the amount of sugar in the spinal fluid in dementia paresis was noted in cases in which pleocytosis was more marked (49 mg., in 52 cases in which the cells were over 30, and 54 mg., in 95 cases in which the cells were below 30). In 61 cases of tabes dorsalis and cerebrospinal syphilis, the average reading for the sugar in the spinal fluid was 59 mg., being 58.7 per cent of the average reading for the blood sugar. In 2 cases of acute multiple sclerosis the reading was 37 and 45 mg., being 45 and 51 per cent, respectively, of the blood sugar value. In 13 other cases of disseminated sclerosis there were normal readings. In 3 cases of tumor of the brain with reactive pleocytosis, the readings were similarly relatively low.

In 56 cases of meningitis the readings for the spinal fluid varied from 12 to 62 mg., the median being  $37.7 \pm 4.5$  mg., in 49 cases the median value for the spinal fluid was 36.6 per cent of that for the blood, ranging from 13 to 65 per cent. In these instances also there was a direct relation between the number of cells and the amount of diminution of sugar in the spinal fluid. No difference was noted between tuberculosis and other bacterial meningitides. Alimentary hyperglycemia in this series resulted in a corresponding increase in the sugar of the spinal fluid, with preservation of the usual ratio. In 17 cases of hydrocephalus and increased intracranial pressure there was a constant increase in the sugar of the spinal fluid—76 mg. (ranging from 72 to 89 mg.), with normal values for the blood sugar. In 7 cases of tumor of the brain, in which the intracranial pressure was increased, there were similar results (from 70 to 83 mg.). The slight increase in the sugar of the spinal fluid in epilepsy, injuries to the head, chronic encephalitis and cerebral arteriosclerosis is of questionable significance and is not statistically reliable. Five double determinations in 2 cases of schizophrenia, with death in catatonic excitement, showed constant hypoglycorrachia (from 77 to 88 mg.). Other investigators have reported a constant increase in the sugar of the spinal fluid in acute encephalitis. No such cases were available during the course of this study. Significant alterations in the sugar of the spinal fluid were not found in various intoxications with industrial poisons (phosphorus, carbon monoxide, magnesium and benzine), in 2 cases of pellagra, in the myopathies, in Friedreich's ataxia, in idiopathic paraparesis agitans and in Pick's and Alzheimer's disease. The only practical clinical application of such studies on the sugar content of the spinal fluid is in cases of bacterial meningitis. The tendency to hypoglycorrachia does not have much clinical value, though it may be used as an indicator that organic disease is probably present.

SAVITSKY, New York.

RELATION OF CEREBROSPINAL FLUID TO POLYNEURITIS. JØRGEN MADSEN, Acta Psychiat. et neurol. **10**:357, 1935.

Madsen reports the cerebrospinal fluid findings in eighty-four cases of various forms of polyneuritis. These included forty-nine cases of toxic neuritis (alcoholism, lead poisoning and diabetes), thirteen cases of infectious neuritis (diphtheria, scarlet fever and acute infection with an unknown type of virus) and twenty-two cases of the cryptogenic form. His findings confirm the observations of Merrit

and Fremont-Smith that the cerebrospinal fluid is nearly always normal in the toxic forms of polyneuritis and nearly always shows the albuminocytologic dissociation of Guillain and Barré in the infectious form. In the infectious form the protein is increased, especially during the acute stage of the disease, the spinal fluid tending to become normal rapidly. In a few cases with an increase in the cell count the clinical findings suggested a meningomyelitic complication of the polyneuritis.

YAKOVLEV, Palmer, Mass.

### Encephalography, Ventriculography and Roentgenography

CEREBRAL ANGIOMAS: THE IMPORTANCE OF CEREBRAL ANGIOGRAPHY IN THEIR DIAGNOSIS. EGAS MONIZ, Bull. Acad. de méd., Paris **113**:174 (Feb. 5) 1935.

Egas Moniz distinguishes three types of angiomas: arterial, venous and arteriovenous. Immediately after injection of thorium dioxide into the common carotid artery, roentgenograms of an arterial angioma can be obtained (arteriography). Films taken four or five seconds later show a venous angioma (phlebography). Egas Moniz recounts the case of a girl aged 16 who had diminution of vision, "neuroretinitis of renal type," with atrophy of the optic nerve and severe headaches and vomiting but no signs permitting localization. Both arteriography and phlebography revealed normal vessels on the right; a large arteriovenous aneurysm was discovered when injection was made on the left side. The arteriogram revealed, in addition to the dilated and abnormal arteries, numerous venous channels already filled with the contrast medium, evidently by direct communication with the arteries. Films taken five seconds later showed the venous portion then filling from the capillaries. The patient was treated by ligation of the common carotid artery, with temporary success. Moniz emphasizes the value of angiography in the diagnosis and localization of intracranial vascular tumor.

MACKAY, Chicago.

VEGETATIVE DISTURBANCES FOLLOWING ENCEPHALOGRAPHY. H. BOETERS, Klin. Wchnschr. **14**:1829 (Dec. 21) 1935.

Duplicate determinations of the sugar content of the blood according to the method of Hagedorn and Jensen were carried out in a series of forty-five neurologic patients before and at intervals after lumbar encephalography. In all cases definite hyperglycemia was noted immediately after the completion of encephalography, the level of the blood sugar after the procedure ranging from 20 to over 100 per cent higher than the initial fasting value. After an hour or two the blood sugar subsided to normal levels. The greatest changes were observed in children, and there was some variation in the degree of hyperglycemia, apparently related to the clinical conditions. Studies as controls indicated that the rise was not due to opiates given before operation or to the action of roentgen rays. Boeters interprets the reaction as a response of the central autonomic centers to the irritation caused by insufflation of air. He supports this assumption by presenting records showing concomitant elevations in temperature, pulse rate and leukocyte count following encephalography. Determinations of the sugar content on fractional samples of cerebrospinal fluid removed during the procedure showed no consistent or significant changes.

BRADLEY, Boston.

AKINETIC STATES FOLLOWING THE INTRODUCTION OF AIR INTO THE THIRD VENTRICLE AND THEIR SIGNIFICANCE. M. GROTJAHN, Monatschr. f. Psychiat. u. Neurol. **93**:121 (May) 1936.

Of a group of eighty-nine patients on whom ventriculography was performed seven presented an unusual and severe type of akinesis. These seven patients, whose ages varied from 7 to 19 years, had slowly growing tumor of the brain,

and all but one showed adiposity of the type associated with dystrophia adiposogenitalis. Prior to the illness, several patients had displayed precocious mental traits, with an even disposition, wittiness and cleverness. In all cases there were marked internal hydrocephalus and papilledema, and with one exception the tumor was located in the suprasellar region or near the aqueduct of Sylvius, the septum pellucidum or the quadrigeminal bodies. As a rule, the akinetic state developed within twenty-four hours after ventriculography had been performed. The patients remained motionless in bed, usually lying on the back, with the eyes open and the extremities atonic. Spontaneous activity was lacking, and automatic movements, such as closure of the eyelids, occurred slowly and with diminished frequency. In one case the state of akinesis was interrupted by short outbursts of singing. By means of vigorous questioning it was always possible to obtain slow, monosyllabic responses. The patients slept well at night. They often fell asleep during the day but could easily be awakened. There was no clouding of consciousness or loss of memory, and cataleptic phenomena were not noted. The vegetative functions appeared to be undisturbed. Incontinence of urine and feces occurred in all cases. The condition was not encountered in patients on whom encephalography was performed, nor did it occur in patients in whom the ventriculography failed to lead to filling of the third ventricle with air. The duration of the illness varied from four weeks to several months. Improvement took place gradually, and in some instances the patients failed to return completely to their previous state of activity. Grotjahn believes that the state of akinesis owes its origin to damage to the gray matter about the third ventricle caused by the ventriculography, but that it is conditioned specifically by the presence of a tumor in that region. The observations tend to corroborate the view that instinctive motility, primitive activity and elementary affectivity, which are closely interrelated, are controlled by the gray matter around the third ventricle.

ROTHSCHILD, Foxborough, Mass.

## Society Transactions

### NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

*Regular Meeting, Dec. 8, 1936*

A. A. BRILL, M.D., *Chairman*

#### A CASE OF NON-NEOPLASTIC SYRINGOMYELIA WITH ROSENTHAL FIBERS: CONSIDERATION OF THE PATHOGENESIS OF SYRINGOMYELIA. DR. AMOUR F. LIBER (by invitation) and DR. JAMES R. LISA.

Rosenthal fibers have been reported in only 6 known cases since their discovery in 1898. It was recently shown by one of us (A. F. L.) that Rosenthal fibers are made up of a substance resembling hemoglobin. These bodies have so far always been observed to exist with syringomyelia associated with intramedullary tumor. For the first time Rosenthal fibers have been seen in a case of syringomyelia in which no tumor was present. A man aged 38, with a probable history of syphilitic infection, died of pulmonary tuberculosis and acute generalized peritonitis following rupture of a tuberculous lesion of the intestine. There was hyperplastic panmeningitis, with adhesions and subarachnoid block in the cervical and lumbar regions of the spinal cord. Diffuse intramedullary breakdown, with peculiar edema and hyaline globes, was present at the third cervical segment. In the lower cervical and upper thoracic regions of the cord the breakdown of tissue merged gradually into a picture typical of syringomyelia with gliosis. Then, after a relatively intact stretch of several segments, diffuse breakdown reappeared in the lumbar region. Rosenthal fibers were present in small numbers at the third cervical segment, in the neighborhood of areas of tissue breakdown without definite cavities or gliosis, and at the fifth cervical segment, in the completely formed glial rings about typical syringomyelic cavities. Breakdown of tissue and syrinx formations were everywhere accompanied by fibrotic thickening of the vascular adventitia within the cord, often resulting in obliteration of the perivascular spaces.

Syringomyelia is probably not a nosologic entity. It may well result from a number of causes and through a variety of mechanisms. The data in the case reported and in some other cases described in the literature suggest the following working hypothesis of the pathogenesis of some types of syringomyelia: Syrinx formation is secondary to destructive stasis of tissue fluid, with cicatricial gliosis. Stasis results from occlusion of drainage pathways of tissue fluids. Adventitial thickening with blockage of the perivascular spaces is the principal factor in impaired drainage. This factor may suffice in itself or may require additional factors, such as subarachnoid adhesions or intramedullary tumor. Various etiologic agents, including developmental anomalies, may contribute one or more of these factors.

#### A CASE OF INTRACRANIAL EPIDERMOID. DR. SIDNEY W. GROSS (by invitation).

Intracranial epidermoid is an unusual neoplasm. In Cushing's series of 2,023 cases of intracranial tumor there were only 12 epidermoids, or about 0.6 per cent. The epidermoid has been called by various names, but the terms "pearly tumor," "cholesteatoma" and "epidermoid" have been used most frequently. The first term refers to the external appearance; the surface often, but not always, looks startlingly like mother-of-pearl. Sometimes the tumor is cystic and contains crystals of cholesterol; hence the term "cholesteatoma." The term "epidermoid" was first used by Bostroem and is preferable from an embryologic point of view, since this tumor, in common with the dermoid, is believed to have its origin in fetal epidermal

inclusions. In the splitting off of the neuro-ectoderm from the ectoderm which forms the skin and in the formation of the neural tube from the medullary plate, inclusions of epidermal cells may occur. The age in fetal life at which epidermal inclusions occur determines more or less the position and structure of the tumor resulting, when for some unknown reason these embryonic rests become neoplastic.

A tailor aged 40 had always been in good health until March 1934, when one day, while at work, he suddenly had a jacksonian seizure involving the right upper extremity. He did not lose consciousness and continued at work when the seizure was over. A few hours later the episode recurred. The next morning, at 3 a. m., his wife was awakened and found the patient in a generalized clonic convulsion. He was comatose for several hours after this. The next day he had no knowledge of having had a convulsion. Twelve hours later generalized convulsions recurred and lasted intermittently for six hours. During the seizures he was incontinent. For the following twenty-four hours the patient had intermittent jacksonian convulsions of the right side of the face, eyelids and mouth, with pulling of the eyes to the right. During the day there developed progressive impairment of speech, and because of this he was admitted to the hospital for the first time, on April 6.

On examination the patient was alert. He was originally left handed but had been trained to write with the right hand. All other skilled acts were performed with the left hand.

The patient was unable to speak in sentences. He named objects correctly after some delay. During the examination frequent twitchings of the right side of the face were noted. The right pupil was slightly larger than the left, and right facial weakness of the central type was present. The tendon reflexes were equal, and there were no abnormal reflexes. Laboratory studies and roentgen examinations gave normal results. Within a few days all the signs and symptoms cleared, and he was discharged as a "brain tumor suspect."

The patient was in apparent good health up to about June 1, 1936, when he began to have persistent dull headaches. On June 15 he had several generalized convulsions, which continued intermittently for twenty-four hours. In this condition he was admitted to the hospital at 5 a. m. on June 16. The convulsions were controlled by intravenous injections of sodium amyital and by lumbar puncture. When examined several hours later the patient was drowsy. He had slight right hemiparesis and was somewhat confused. Within forty-eight hours all these signs and symptoms cleared, and the patient seemed well. Examination of the visual fields and laboratory studies disclosed no abnormalities. The spinal fluid was clear and colorless. Pressure was 150 mm. of water; the chemical composition and serologic reactions were normal.

An encephalogram made on June 20 showed the entire ventricular system to be displaced slightly to the right. An oval collection of air was found in the left frontal region, depressing the anterior part of the left lateral ventricle.

A left frontal craniotomy was performed with local anesthesia on June 24. In the anterior part of the left middle frontal convolution, about 2 cm. below the surface, a cystic tumor was observed. On aspiration a slightly turbid fluid containing crystals of cholesterol was obtained from the interior of the cyst. The capsule of the tumor was incised, and after removal of a waxy, yellowish material, the capsule was teased out. Up to this point the removal of the tumor was practically bloodless. The capsule at one point was attached to the choroid plexus, and removal of this bit of capsule was followed by brisk hemorrhage, which, however, was easily controlled. It was evident that the cyst communicated with the lateral ventricle.

For the first few days after operation the patient was aphasic and had complete right hemiparesis. Speech and motor power returned rapidly, and he was discharged from the hospital on July 9. He soon returned to work and at present considers himself well.

*Comment.*—Most epidermoids heretofore described have been in more or less intimate contact with the pia-arachnoid, many of them arising in the subarachnoid

cisterns. The sites of predilection were the fourth ventricle, the cerebellopontile recess and the suprasellar region. Cushing described a large extradural epidermoid which eroded the inner table of the skull extensively. Critchley and Ferguson observed 8 epidermoids in the large collection of tumors of the brain in the National Hospital, London. All the patients in their series were males. In 1 instance the tumor was cystic and subcortical and closely resembled that in the case which I am reporting.

Bailey's account of the histologic picture of the epidermoid is classic. He described it microscopically as "looking like the cross-section of a dead plant." The capsule of an epidermoid consists of strands of connective tissue. Its interior is made up of inert, lifeless material, devoid of blood vessels. Below the capsule a homogeneous, structureless material is present. This has a waxy, flaky feel, which is characteristic of the epidermoid.

This homogeneous material makes up the stratum durum of Bailey. The stratum granulosum and stratum fibrosum consist of layer after layer of easily separated lamallae. The stratum cellulosum makes up the bulk of the tumor and consists of aggregations of flat, polyhedral cells, having definite cell boundaries but poorly defined and pyknotic nuclei.

In a condition diagnosed as tumor of the brain, if, in addition to the location, the surgeon has some idea of the probable nature of the growth, he is better prepared to cope with it. It is often possible to predict with a reasonable degree of accuracy the probable histologic character of many tumors of the brain. This is especially true of tumor of the acoustic nerve and of some meningiomas which produce rather typical clinical syndromes and changes in the roentgenogram.

The epidermoid occurs infrequently, even in large clinics, so that a preoperative histologic diagnosis is rarely made. From the congenital origin a long history might be expected, and this is borne out in many cases reported in the literature. Olivecrona made a correct preoperative diagnosis of a suprasellar epidermoid in a young woman with slowly progressive primary atrophy of the optic nerve and enlargement of the optic foramina, with a normal sella and absence of signs of disease of the pituitary gland. He had, however, noted a similar combination of symptoms in a patient in whom the diagnosis was made at operation only a few weeks before the second case appeared.

Of all intracranial tumors the epidermoid has perhaps the best prognosis. Because of its slow growth, signs of increased intracranial pressure are mild or absent. The tumor is practically avascular; hence, it is usually easily removed completely. If extirpation includes the capsule, it tends not to recur. Cairns, in his analysis seven years later of all patients operated on during his year in the Cushing clinic, found that both patients who had had an epidermoid removed were in good health and gainfully employed.

#### CALCIUM THERAPY IN HYPERTONIC COLOPATHY: CLINICAL OBSERVATIONS. DR. THEOPHILUS P. ALLEN.

Ninety-eight patients with chronic or remittent diarrhea of unknown origin were treated with intravenous injection of calcium gluconate, and oral administration of dicalcium phosphate ( $\text{CaHPO}_4$ ) and vitamin concentrates. This is the treatment usually given in tuberculous enteritis. Seventy-eight per cent of the patients were clearly benefited. The intravenous injections were followed by cessation of symptoms in from fifteen minutes to one hour, and relapses were repeatedly controlled by subsequent injections. Dietary restrictions were minimal. Most of the patients were already receiving low residue diets, and no change was made. Two patients given average diets were relieved without changing their eating habits. When patients failed to respond to intravenous injection of 1 Gm. of calcium gluconate, doubling or tripling the dose and adding parathyroid extract brought no additional improvement.

Analysis of the group of patients who were benefited as compared with those who did not improve seems to indicate that sex, duration and severity of the illness and tolerance to milk had little or nothing to do with the therapeutic

response. Of the group who were benefited 53 per cent had evidence of allergy, and the average age was 49 years. Of the group in which treatment failed 33 per cent had evidence of allergy, and the average age was 40.1 years.

Fifty-eight patients with acute diarrhea, usually typical gastro-enteritis, were treated with one intravenous injection of calcium gluconate. Ninety-one per cent of these patients were clearly benefited. Usually no other treatment was given.

The characteristic effect of increasing the calcium ions in perfusing fluid is to lessen neuromuscular irritability, and since 70 per cent of the calcium given intravenously is excreted into the bowel, the effect would be most evident there. In simple hypertonic colopathy one may presume the exciting agent to be diffuse and the activity of the intestine to be generalized arrhythmia or fibrillation. Desensitization by excess calcium may restore normal rhythm to the bowel, as does quinidine sulfate to the fibrillating auricle.

#### DISCUSSION

DR. LOUIS CASAMAJOR: When Dr. Allen asked me to discuss his paper, I said yes; I should not have done so, for I do not know anything about calcium. I have read a good deal and listened more, and still I do not know anything about it. Hence, my remarks tonight will be brief. I was interested in Dr. Allen's work because of a patient in whom he obtained brilliant results which I had been unable to achieve over a number of years. This patient was a woman of charm and culture, with an astoundingly unstable emotional fabric. When she was emotionally unstable, she had diarrhea and considerable pain and passed large amounts of mucus. I was unable to approach her by any psychologic means. The internist who had tried to work with her had given her considerable phenobarbital and camphorated tincture of opium, with no brilliant results. On one occasion it was discovered that a cystic ovary, on the right side, was giving symptoms, and laparotomy was performed. The colon was observed to be extremely thin walled and very large. The surgeon took a tuck in the colon, but the diarrhea was not in the least influenced. Some time after, Dr. Allen saw the patient and by means of calcium therapy achieved a good result. The patient still has diarrhea, on a definitely emotional basis, but by the use of intravenous injections of calcium Dr. Allen has been able to check it when it occurs. It is impossible to prevent it altogether, but when it does come, he has been able to reduce the number of movements in any one period of twenty-four hours. I have always had a doubt in the back of my mind as to whether Dr. Allen achieved this result by means of the charm of his personality or by the calcium. He says it is by the calcium.

Those who are practicing neurology or psychiatry know how difficult these conditions are to treat. They are due fundamentally to emotional causes and their basis is not unlike that in the fear type of diarrhea. In fact, it is usually connected with the emotion of fear; when once started, it continues, until one feels that there must be established in these cases a vicious cycle.

There are definitely a mental and emotional level, an autonomic level and a glandular and biochemical level. One feels that in treating such conditions one might break in at one of these three levels. One tries to break in at the emotional level by means of psychotherapy, usually with results that are nothing to boast of. Dr. Allen succeeded in this case in breaking in at a biochemical level. All remember that in the early textbooks on neuroses many hundreds of types of neuroses were described, before the basis of the neurosis was understood as it is today. Among these types were the organ neuroses, which were thought not to have anything to do with the mind. There were bladder neuroses, heart neuroses, and so on. One now looks on the organ neuroses, of which this condition is an example, as expressions in the organic field of an emotional upset of some sort. One does not like even to call this reaction unconscious. It seems something much lower than the unconscious. It comes much closer to the more primitive types of life. It is a mental reaction, yes, but a mental reaction like nothing in the mental sphere. It is a psychologic reaction entirely in a biochemical sphere. When one looks on the problem from that point of view, one can see why it is possible to obtain such a result as Dr. Allen has shown tonight. I know from

this case and from examining Dr. Allen's statistics that it is possible to break in at this level and to bring about reactions in situations that are essentially emotional by means of a biochemical substance, especially calcium.

If some one will tell me how calcium works in these cases and why, perhaps I shall learn something about calcium.

DR. ROBERT F. SOLLEY: I am sorry that I cannot tell Dr. Casamajor anything about calcium or why it works or what it does. There has been a great deal of conversation in the literature and in physicians' coat-rooms about calcium and other minerals. There is a large literature dealing with the absorption of calcium and deficiency of calcium in the diet. The use of calcium, as Dr. Allen has outlined in the treatment of these colopathies, especially the diarrheas, is interesting not only because it attacks the biochemical aspect of the problem but because it has, I think, a strong psychotherapeutic effect. Patients like to have something concrete done. To the average patient nothing in the realm of medical therapeutics compares with being stuck with a needle and seeing the bright red blood flow into the syringe. It has a strong effect, I think, but of course this is not the whole matter. I have often tried to undermine the confidence of patients in the treatment with calcium, in order to see the physiologic effects of the calcium alone. In 5 or 6 instances patients have benefited from calcium in whom I have tried to undermine the suggestive effects as much as possible. I have told some that it was just a test and some that I had no particular faith in the substance. On the other hand, there is a strong psychotherapeutic element, I am sure. I was fortunate to have the opportunity to treat several of Dr. Allen's patients when he was on vacation, and 2 of those who had responded magnificently in his hands failed to do so in mine.

As concerns the absorption of calcium in the average adult human subject—these patients are all adults—and the calcium reserve, a point, I think, is of use: Most persons who respond to this treatment are in the older age groups—past the third decade of life. As persons go on in life, they drink less milk and achieve a certain calcium deficiency, if that exists. Also, in many elderly persons with diarrhea there is achlorhydria, and with achlorhydria the absorption of calcium is even less than in persons with a normal amount of hydrochloric acid in the stomach. That is the only chemical contribution that I can make to the subject.

DR. A. A. BRILL: So far nobody has explained how calcium therapy actually works. Dr. Casamajor went so far as to put its efficacy below the level of the unconscious, and Dr. Solley stated that he tried hard to destroy the patient's faith in the suggestion of the needle, which, he justly believes, plays a part. I am, however, anxious to learn something about the modus operandi of calcium therapy. I, therefore, shall ask Dr. Bernheim to explain, if possible, how calcium works.

DR. ALICE R. BERNHEIM: Perhaps the effect of calcium may best be explained in terms of its action on single cells. Calcium decreases cell permeability. According to Bayliss, a too permeable cell is an irritable cell. Calcium thus makes cells less irritable. However, in many cases in which calcium therapy is effectual, there is no reduction in the calcium content of the blood. The concentration of total calcium in the blood is remarkably constant. It would seem that the blood must have its 10 mg. of calcium per hundred cubic centimeters, and since the body does not make calcium, it must come from somewhere. Ordinarily, calcium is supplied to the blood from the bones and the food. It is interesting that the calcium which comes from the bones and passes into the blood does not go back to the bones but is excreted, largely in the feces, while the calcium which is absorbed through the digestive tract into the blood is deposited in the bones and the portion which the bones do not take is excreted largely not in the feces but in the urine. The calcium from the bones thus behaves differently from the calcium that is absorbed from the digestive tract. The difference in their behavior suggests that they may, indeed, be different forms of calcium. There is, however, no direct evidence to show that they are.

There is more than one form of calcium in the blood. The recent work of McLean and Hastings indicated that there are only two forms: the nondiffusible, which is bound to protein, and the diffusible, which is the available, active form of calcium.

Klinke, Greenwald and others, however, expressed the belief that there are three forms of calcium in the blood. By electrolytic experiments they have shown the diffusible calcium to be present in two forms: one positively charged—the available calcium—and the other a complex form negatively charged and not available. Hess and Benjamin stated that there are four forms of calcium in the blood.

I was interested to hear that Dr. Allen obtained such good results from the administration of dicalcium phosphate, since it is usually poorly absorbed. As Dr. Solley said, the question of absorption is one of great importance in oral calcium therapy.

DR. IRVING H. PARDEE: All are grateful to Dr. Allen for speaking on a subject which is close to neurologists and psychiatrists. Many psychoneurotic patients have colitis as part of their clinical picture. Whether the colitis has an emotional or a vegetative background or both I do not see that there is any particular reason for deciding. It has probably both. The point in Dr. Allen's paper in which I am especially interested is that he says he cures some of his patients. I had almost reached the belief that there are few patients with colitis who recover. I thought: Once colitis, always colitis. To be sure, the patient may get better and reach a certain level at which he can live and be reasonably comfortable; nevertheless, the colitis, I thought, was always in the life and background of the constitution of that patient.

There is another point about which I wish to ask Dr. Allen: Is there a rhythm to colitis? Has colitis a weekly, a semimonthly or a monthly rhythm? Is there any rhythm? Is there any relation of colitis to the menstrual cycle? Is there the relation in the male also to a theoretical twenty-eight day cycle?

If calcium has a local effect on the intestinal tract, why do you give it intravenously so invariably, when in nine of ten patients there is an adequate response to oral medication? Personally, I do not believe in the psychotherapeutic effect as strongly as Dr. Solley does, for most patients are educated to needle therapy in these days and the suggestion from it is fairly limited.

I look on patients who have colitis as persons with a certain constitutional make-up. Just what that constitution is will require a great deal of thought and study, but the subjects are usually the persons of the long, thin, ptotic type, who are prone to intestinal spasticity and muscular or myotatic irritability. These are the patients who are known to be low in calcium. Whether they are of the thymic, or status lymphaticus, type is still a question for further study.

DR. THEOPHILUS P. ALLEN: I carefully avoided the use of the word "cure," Dr. Pardee. One man has been for five years without any significant recurrences for as long as he takes dicalcium phosphate by mouth, but if he stops it the diarrhea tends to recur. In my best results, in cases of long-standing diarrhea, this has eventually happened. The patients reach the point of controlling the diarrhea with dicalcium phosphate without intravenous therapy.

I am agreeable to the point which Dr. Bernheim made about dicalcium phosphate; I mean I believe that dicalcium phosphate acts locally on the bowel, as kaolin or any other insoluble powder might, with a mildly constipating effect.

I tried to connect the diarrhea with the menstrual cycle, without any demonstrable success, but in some cases it seemed that the diarrhea was better after the menopause. In one girl the diarrhea disappeared after surgical removal of the ovaries, followed by hyperthyroidism. Even after she had hyperthyroidism, there was no recurrence of the diarrhea. She was treated with roentgen rays, and the basal metabolic rate fell from plus 40 to minus 5. She gained weight and has been free from diarrhea since, but is as neurotic as ever.

As for the constitutional types: Certainly, the average patient is the thin, ptotic type, but I have had 3 or 4 definitely obese patients with diarrhea who responded to the injections. However, all the anthropologic types were involved.

Three patients with hyperthyroidism responded, and at least 5 or 6 with definite neurasthenia, that is, with slow pulse, low blood pressure and mild hypothyroidism, reacted equally well. I believe that the disorder is constitutional but that it is not limited to any definite type.

I do not profess to be much of a scientist, but for purposes of my own thinking, it seemed that the best way to understand how calcium may work in such diarrheas is to visualize the effects of perfusing a heart with Ringer's solution. Increasing the calcium ions eventually brings the heart to a stop in calcium rigor, that is, in systole, but before that point is reached, it slows the rate and increases the amplitude of the beat. The other pharmacologic actions of calcium are: Excess calcium in the perfusing fluid antagonizes the effect of pilocarpine; deficiency of calcium in the perfusing fluid reverses the characteristic action of atropine. Calcium is antagonistic to ergotamine and is an antidote for ergotamine poisoning. The presence of calcium in the perfusing fluid is necessary for the characteristic vasoconstrictor action of epinephrine. As Dr. Bernheim said, 70 per cent of the calcium is excreted through the bowel. In giving calcium intravenously one has the set-up of a physiologic experiment—with a perfusing fluid in which the number of calcium ions has been increased. It can then exhibit its characteristic effect of reducing neuromuscular irritability. Analysis of this group of pharmacologic phenomena would make one think that the effect is sympathetico-tonic, and perhaps it is.

Some of the hormones and minerals must be closely interrelated and dependent on each other for their characteristic activity. Some diarrheas are on an emotional basis. When one is in a state of emotion, one may have some hormonal imbalance—perhaps a deficiency but usually an excess. It is possible that the excess calcium at that time would supply the principal needed and bring about some kind of autonomic balance by a synergistic action with the hormones. This, of course, is pure speculation.

#### JUDICIOUS SELECTION OF PATIENTS FOR PSYCHOANALYTIC THERAPY. DR. SÁNDOR LORAND.

Two patients with neurotic depression bordering on melancholia had been given more than three years of psychoanalytic treatment. There is necessity for careful selection of patients suitable for psychoanalytic treatment and for criteria to guide in the selection. All patients suffering from depression must have had a childhood neurosis, which provided fertile soil for the depression in adult life. To expect favorable results from analytic treatment in such states, a degree of stability must be present in the patient's character. Too much elasticity and instability make the condition unsuited to the psychoanalytic approach, for the regressive tendencies are too strong.

Patients who show psychotic trends and those with manic-depressive psychosis, schizophrenia and severe alcoholism should not be experimented with in psychoanalysis, except in closed institutions. There, attempts may be made to help them with a modified, individualized technic; this is, by the way, also true to an extent of the treatment for depressive states. In the "New Introductory Lectures," Freud strongly advised against experimenting with psychotic patients.

The present paper was written with the aim of refuting the concept that psychoanalysts are unaware of any limitations and that they treat at random all kinds of conditions, even psychoses—a view recently expressed by Dr. H. T. Hyman (*The Value of Psychoanalysis as a Therapeutic Procedure, J. A. M. A.* **107**:326 [Aug. 1] 1936). In this paper statistics purporting to show the failure of psychoanalytic therapy were based, for the most part, on results obtained from the attempted analysis of obviously psychotic patients.

#### DISCUSSION

DR. CLARENCE P. OBERNDORF: The title of this paper has a reminiscent note, because, I think, the question of the judicious selection of patients for psycho-

analysis has been presented in this building and in certain other places annually since Dr. Brill brought psychoanalysis to the United States, about thirty years ago. Psychiatrists should appreciate that Dr. Lorand has brought up this subject again, in view of the acrid attack made against psychoanalysis here last spring. It would be cogent to discuss not the psychoanalytic theory of depression and its relationship to the multiform picture which Dr. Lorand's patients presented but the subject included in the title of the paper, which is the judicious selection of patients for psychoanalytic therapy. This involves three factors: the meaning of the word psychoanalysis, the types of patients and judiciousness in their selection.

The term psychoanalysis is used in many ways. Indeed, the concept of what psychoanalysis is at times appears nebulous in the minds of some persons. Only a short time ago I went to one of the wards of a general hospital, in response to a note requesting a consultation. The intern politely asked me "to make a psychoanalysis of the patient at once," as he was leaving the hospital that afternoon. That was his conception of psychoanalysis. In contrast to this, treatment in Dr. Lorand's cases covered three years—not an uncommonly long time for psychoanalysis.

The term psychoanalysis is used in several ways. First, it is employed to denote the theory of Freud as to the relationship between conscious and unconscious mentation. Second, it is used to denote a form of treatment, and, third, the technic of that treatment. Treatment and technic are, of course, closely related. However, even when one uses the term in the sense of treatment and (or) technic, one must qualify it, since there exists in treatment the range of partial analysis, orthodox analysis, reeducation on psychoanalytic principles and trial analysis for diagnostic purposes. If, then, one is to evaluate psychoanalysis, one must know what kind of psychoanalysis has been undertaken, and to what degree—not to mention the degree of skill with which it has been employed.

The second factor is the patient. The conditions to which psychoanalysis is applicable are varied; personally, I should be inclined to do away with such terms as schizophrenia, manic-depressive psychoses, neuroses, psychoneuroses and conversion hysteria, except for descriptive purposes. Of course, all patients must be intelligent and reasonably desirous of getting well. The availability of patients for psychoanalysis depends on three factors: first, the presence and depth of insight; second, the possibility of a steady, consistent and active transference in its positive or negative phases, and, third, the degree to which the patient has denied reality.

One can readily see that these three factors may be variable. In certain patients, especially those whom one designates, for descriptive purposes, as schizophrenic or manic-depressive, some or all of these factors are lacking. Many paranoid and many schizophrenic patients lack insight. If insight is persistently wanting, there is no use in undertaking the treatment. So also, deep transference is impossible for manic patients. Their distractibility and flightiness make it impossible for them. Schizophrenic patients are too devoted to themselves to make a transference.

When one considers the relation of the patient's mental state to reality, one finds not only that the depressed patient is so engrossed in depression that he cannot transfer but that he may not realize that many of his complaints have no basis in fact. With paranoid patients and those with the hallucinatory mechanisms that appear in the graver forms of schizophrenia, the distortion and denial of reality make the psychoanalytic approach extremely unfruitful.

It is also true that in many, perhaps in most, cases in which analysis is made the diagnosis of psychosis or neurosis would depend on which phase of the illness the analyst singled out. I think that both Dr. Lorand's patients had delusions and were depressed. One certainly had a pronounced compulsion neurosis. The "diagnosis," therefore, depends largely on which features in the psychic picture the physician wishes to emphasize—whether he labels them psychosis or neurosis.

The third point is judiciousness in the selection of patients. Dr. Lorand, I think, made the statement that Dr. Hyman should have known which patients to send to the analyst. It seems to me the shoe is on the other foot—that the analyst should have known which patients to reject. The fault is with the analyst, who continued to treat the patients whom he did not think were suitable for analysis.

As to the possibility of cure: One comes here to another variable factor. "Cure" is a relative term. Indeed, one cannot speak of "cure" in psychoanalysis in a circumscribed sense. The criteria for cure which I set for myself are: (1) disappearance of symptoms, (2) fair insight into the unconscious mechanisms that caused the symptoms to occur and (3) satisfactory adjustment to heterosexuality and the environment.

Therefore, one can see the difficulty involved in approaching psychoanalysis on a statistical basis. Dr. Hyman has performed a service in calling the attention of the medical profession to what can be expected when a patient is referred for analysis as to the result, the degree of the result and the length of time required for treatment. It is difficult to say in any particular case how long a time will be required for tangible improvement, and often this can be determined only after a considerable period.

If one attempts to approach this matter from the statistical point of view, one has to consider too many variables ever to arrive at intelligent conclusions. However, another yardstick is the cumulative experience of qualified men. They affirm that by this method benefits have been accomplished that were unknown in pre-analytic days—both in specific psychoneuroses and in conditions which verge on schizophrenia, on the one hand, and on manic-depressive psychosis, on the other. I think it is also true that even with severely involved schizophrenic patients intelligent reeducation based on analytic interpretations is of great value, both in institutions and outside.

If statistical data are not possible, analysts at least can and should pool their accumulated experience, so that the public may know what to expect from the method. Such an attempt was initiated by Dr. Edward Glover several years ago by means of a questionnaire sent to various analysts, in order that he and they might orient themselves as to the results to be expected. The replies were extremely varied, and a summary of these results has not yet been published.

Finally, I should say that psychoanalytic experience is not limited to New York City or to America but that analytic societies range from Tokyo to New York and from Oslo to Capetown. Further, there will be an increased need for judging what conditions are suitable for analysis, for there are at present nearly fifty physicians, well qualified in psychiatric work, in training at the New York Psychoanalytic Institute to become psychoanalysts. With that great number of analysts in the offing in one locality, one must be even more sure, cautious and judicious in selecting patients in the future, and one must not encourage the application of the method in situations in which the outlook is inauspicious. This, it seems, can be determined only as a result of the combined experience of competent analysts, who impart their knowledge to younger men—not through statistical tables.

DR. DAVID M. LEVY: Psychoanalyzability is a convenient term, which probably covers the problem for discussion this evening. It refers not only to the treatment of psychosis but to that of neurosis, for there are a number of psychoses in which analysis is easier than in certain severe neuroses; i. e., certain psychoses are more amenable to psychoanalysis than certain severe neuroses. In the selection of patients for analysis one needs to establish criteria and careful follow-up studies to determine how well the subject can differentiate, a sufficient degree of skill on the part of the analyst being assumed. There are no criteria at present that are determined empirically. I disagree with Dr. Oberndorf that it is not possible to make a statistical study of prognostic features in analysis. It can be done. Dr. Oberndorf hoped to initiate such a study but was unable to secure cooperation. All utilize, nevertheless, certain definite judgments about prognosis in analysis. There is a helpful device to assist one in this task. I refer to an ink spot test,

the Rorschach test, devised about thirty years ago and in use since. The man who has utilized the test for this purpose and has tried it out to the fullest degree against the results of psychoanalytic therapy has not yet published his findings. I have no such data, but the scheme for determining psychoanalyzability according to the test rests, nevertheless, on sound clinical wisdom. I present it in its simplest form. A patient who is to be psychoanalyzed ought to possess these qualifications: He should be intelligent, stable and flexible, and he should have insight.

First, as to intelligence: One cannot analyze the feeble-minded because they have not sufficient intelligence to understand the procedure. Even analysis of the dull normal person is difficult, because of lack of adequate conceptual material. I speak, of course, of the usual analytic procedure. As regards stability: One will not analyze psychoneurotic or psychopathic personalities in which impulsive "acting out" or marked instability has featured their lives. In regard to the rigidity of personality: One will not psychoanalyze, for instance, a man of 80, however mild the neurosis. The age factor itself will give an example of what is meant by rigidity. Some persons cannot be modified by therapy because the neurosis is too well preserved in the personality—too powerfully crystallized. They represent the antithesis to instability. Finally, in regard to insight: One must consider peculiarities of the personality such that replies to the ink spot test, consistent with the evaluation of behavior, are peculiar and bizarre and so out of focus that they may not yield one of the numerous "usual" responses to the test.

I have oversimplified the criteria by omitting much necessary elaboration. They are to be regarded as having a quantitative aspect and to be evaluated in terms of the entire clinical picture. Experience in using the test seems to indicate that the ordinary psychoanalytic method is not appropriate in most cases of schizophrenia, in many cases of psychopathic personality and obsessional neurosis and in certain cases of hysteria. The question of transference is comprehended by the factors already enumerated.

In regard to Dr. Hyman's patients: A number of them, I believe, were never thought to be good prospects for analysis but were accepted on an experimental basis, for most persons, when given a choice between psychoanalysis and institutional, custodial care for schizophrenic patients, would, I am sure, prefer analysis, on the chance that the patient might be benefited, and yet would recognize the need of altering the technic. When one can study the reliability of prognostic criteria through the basic test of statistics on psychoanalytic therapies, one will be able to speak with some degree of accuracy of the selection of patients for psychoanalysis.

DR. ADOLPH STERN: This subject has been thoroughly covered tonight; I wish to summarize, in a sense, on the basis of what has been said and of my own experience. As I see it, the difficulties are due to a transition. One has been accustomed to analyze and work with persons with transference psychoneuroses. That is how one started years ago—those who began then. Other things were ruled out as a matter of fact, but it was not possible to leave out of consideration all persons who did not have a straightforward psychoneurosis. They came for treatment, and one had to look after them because they were sick. In days gone by I did not analyze them. Later, I analyzed some, and later, more of those whom previously I had not analyzed. On what did I make the transition from the straightforward psychoneurosis to the borderline conditions? I exclude the straightforward psychoses. I should not think of analyzing a patient with schizophrenia or manic-depressive psychosis, especially the frankly manic or depressive type, but there are a vast number of persons who need treatment, who come for treatment, who are entitled to it and who can get help, I think, through analysis, without variation of the technic from the Freudian method. A factor that enters here is narcissism, as I see it. It is a new factor. One has been brought up to fear narcissism, as a matter of fact—to think that one could not treat it or work with it. That is not true. One reason that one did not treat

narcissistically involved persons before is that one did not know how to manage one's own narcissism in the face of the problem—that the patients present differences from the straightforward psychoneurotic personality. There are certain criteria by which one can judge these persons, too. These criteria are not hard and fast. One cannot help all the patients whom one undertakes to treat. Some can be helped a good deal, and some can even be cured. If the prognosis is to be good, the patient should have a quantity of ego functioning unininvolved in his character traits, in his neurotic traits or in his psychotic manifestations. This is equally true in the transference neurosis, because the one thing on which one can work and through which one can hope to get results is the intelligence of the patient. The intelligence must be unimpaired, except as it may be impaired through anxiety, so that one can enable that ego to function, in order that the patient can understand what one is telling him with reference to his own difficulties. That is the agent in the cure of the psychoneurotic patient, and the only agent through which one can reach narcissistic persons who make up this borderline group.

These narcissistic persons may not have as much insight as one would like, but sooner or later one must feel sure that one can achieve insight for these persons into the phenomena that they present, some of which they may not be conscious of. Many of these persons present a rigid personality. Dr. Levy thinks that rigid personalities are not amenable to analysis. I agree with him in the main that they are not, but when the rigid personality is symptomatic—a defensive rigidity against a deep anxiety that is almost organic and is fundamentally constitutional and not libidinal in the sense in which one is accustomed to see it in the straightforward psychoneurosis—it may not be evident at first, and one may feel that the patient is not analyzable. This rigidity is comparable to that of the schizophrenic patient in his defense against the anxiety which he believes threatens his very existence. In days gone by I rejected patients like this as not amenable to psychoanalysis. If one is to obtain more from analysis now than in the past, one can do so only by trying new things. One must be judicious. Experience shows that. Patients with rigid personalities have masochistic phenomena which present almost malignant aspects. They have no insight into their feelings. They mask hypersensitivity with rigidity, as a protection against repeated injury of the hypersensitivity. Even ten years ago I did not analyze these patients. I did not know what the phenomena meant. I was not familiar from a therapeutic point of view with the manifestations of narcissism and masochism. These are the two new phenomena which these borderline psychoses present, and I should advise working with the patients with all the judiciousness one can bring to bear.

DR. A. A. BRILL: No matter how long the discussion continues, it will always come down to the question of the psychoanalyst. I believe that if he knows the pathologic and psychologic aspects of the mind, that is, if he has had the proper training for this therapy, he will know what to do with his patients. No two patients are alike, whether they have a transference neurosis or a psychosis. As in medicine and surgery one cannot always find in practice what one was taught in school and hospital work, so in psychotherapy one learns through experience how to manage the individual patient. A properly trained analyst will know what is suitable for this therapy. I agree that Dr. Hyman is not to blame. I should like to know what kind of an analyst treated his patients. I doubt whether any trained analyst would have taken psychotic patients for analysis without telling Dr. Hyman the true situation. I take such patients as those mentioned by Dr. Stern. One has to take them. If psychiatrists, psychotherapists and psychoanalysts can keep such patients out of institutions they should do so, but they should be explicit with the relatives and the physician who recommends the patient.

DR. SÁNDOR LORAND: I thank all the discussers who have helped to widen the scope of my paper. The reason that I wrote this paper is exactly that which Dr. Brill has given. The patients were not suited for analysis, certainly not for statistical purposes; so one should not be called names for having had this unfortunate experience with them.

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ORIGIN AND NATURE OF HYPOGLYCEMIC THERAPY OF THE PSYCHOSES. DR. MANFRED SAKEL, Vienna (by invitation).

Three and one-half years have passed since I first reported a new method of treating psychoses to the Medical Society of Vienna. The treatment was new not because it used a new substance (insulin) but because it involved the deliberate use of the hypoglycemic state, which had been regarded as dangerous by most physicians.

The idea of treatment with hypoglycemic shock for psychoses goes back to 1928; in succeeding years the therapy was developed to the point at which it could be practiced in a way I described in my monograph (*Neue Behandlungsmethode der Schizophrenie*, Vienna, M. Perles, 1935).

This treatment was based on the logical consequence of the idea which led me to introduce moderate doses of insulin in the treatment of addiction to morphine. The observations I made in a few instances of accidental deep hypoglycemia in the treatment of drug addiction encouraged me to attempt the use of hypoglycemia as such in the treatment of psychoses; for the changes I saw in the mental picture both during and after deep hypoglycemia were surprising and demonstrated to me beyond a doubt that hypoglycemia either directly or indirectly can influence psychotic states in a way that may be put to practical use.

It was at this point that I made the transition from the insulin to the hypoglycemic treatment of psychoses. Before a useful form of treatment was evolved, however, it was necessary to develop a method by means of which one could reduce to a minimum the possible dangers—which were overestimated at that time. A technic had to be established which could avoid or prevent danger.

Therapeutic results depend not only on the production of a hypoglycemic state but on the proper use and management of every hypoglycemic shock. They depend not on the size of the dose of insulin but on the timely termination of each hypoglycemic state. Psychologic considerations are important throughout the treatment. All know that in mental and physical diseases psychologic factors not only are of interest per se but can produce pathologic changes through the vegetative nervous system and indirectly perhaps even anatomic changes.

When the treatment was first developed, I could not say exactly why I terminated the hypoglycemia at one point in one case and at a different point in another or why I varied the period of hypoglycemia in the same case at different stages of treatment. The probability was that I was guided by dim unconscious recollections of previous experiences in similar cases. It was only after a time that I was able to indicate in a general way certain principles of management for different groups of patients, and I hope that in spite of the difficulties involved in the treatment these guiding principles will permit a wider application of the method. It should not be forgotten that this treatment is not merely pharmacologic. Before the therapeutic possibility of hypoglycemia can be explored, the method must be learned, just as an operative technic has to be mastered.

As treatment progresses, the lucid phases produced by hypoglycemia become more and more protracted and finally begin to outlast the period of hypoglycemia. The patient then remains free from hallucinations for a considerable time. Patients who are progressing favorably remain free from symptoms throughout the day, until the treatment on the following day; that is, they are without hallucinations and show insight into the illness. At this point a curious thing happens. The patient, who at the beginning of treatment had lucid periods only during hypoglycemia—to become psychotic again at the end of the treatment—for the first

time becomes free from symptoms throughout the day but begins to show psychotic symptoms again for a brief period during hypoglycemia. In other words, there is a reversal of reaction.

Hypoglycemia at first revives the normal personality of an acutely psychotic person. Later, when the patient has improved, the hypoglycemia helps to revive the psychosis, which had been repressed but not yet eliminated. However, these psychotic periods of hypoglycemia are soon shortened and finally eliminated, so that the patient is at last free from symptoms, both during hypoglycemia and thereafter.

In summing up this superficial description of the patient's reaction to hypoglycemia, one obtains the following impression: The hypoglycemic state weakens, inhibits and finally represses the portion of the mind which happens to be most active at the time, so that the hitherto latent, subdued and repressed elements are again brought to the surface, to prevail again over those which are now repressed. This is particularly clear when the hypoglycemia reaches its greatest intensity, just before the onset of coma. In conditions which run a favorable course, the repeated hypoglycemic states finally eliminate the psychosis, so that the normal personality can again achieve complete dominance.

It is not merely my own impression that prompts me to say that anybody who has sufficient experience with the treatment and some insight into the phenomena must recognize that hypoglycemia has a special influence on psychosis. One cannot escape the impression that one can deliberately influence the nucleus of the psychosis by hypoglycemia.

My personal experience now includes over 300 patients, and already as many more have been treated by others. I am aware of the difficulty in reducing the material to statistical study, so that this new treatment for schizophrenia can be evaluated. The natural fluctuations which occur in the course of the disease, the absence of the definite symptoms that one observes in physical disease and the impossibility of making a certain prognosis in any case—all make it difficult to estimate results, especially when the case material is small. My series of cases and those of others indicate, however, that the net result is a percentage of remissions which is at least four times as great as the most optimistic figures for spontaneous remissions. In view of this, I think one is entitled to conclude that the treatment is effective. In estimating the results of this treatment, one must distinguish between recent conditions, of no longer than six months' duration, chronic conditions, with a duration of over a year and a half, and the group between, with a duration of from six months to a year and a half. I attach particular importance to the concept of a full remission. A full remission means not only that the patient is free from symptoms after treatment is concluded but that he has full insight into his illness, that his emotional reactions are normal and that he can return to his work.

In addition to a full remission, I speak of a "good" remission—that is, a condition in which the patient is free from schizophrenic symptoms and can resume his work but has a slight degree of defect. Finally, I speak of a "social" remission. The concept of mere improvement has not been used in formulating the statistical results.

After defining these concepts and reviewing carefully my first group of over 100 patients, I find the following results: Of patients with recent illness 88 per cent had a good or a full remission and could return to work. Of these 70 per cent had a full remission. In all other patients, that is, in all patients the duration of whose illness was over six months, the results varied in direct relation to the duration of the illness. In my material 47 per cent of the patients showed good remissions with capacity to work, of which 19 per cent were full remissions.

When one examines the statistics for spontaneous remissions in schizophrenia for various countries, one finds that the figures vary from 5 to 20 per cent, according to the author. Even if one compares the percentage of remissions after treatment with the optimistic figure of 30 per cent, there is still a large balance in favor of the treatment.

I wish to add that I used to think that only recent conditions would show a satisfactory response to treatment. Later I realized that in some chronic con-

ditions—not in all—some improvement is possible and is worth seeking. It is not a matter of indifference that the chronic forms can be improved. When one considers how serious a problem chronic schizophrenia has become and how much can be done to improve these conditions, the effort seems well worth while.

At the invitation of state commissioner Dr. Frederick W. Parsons, I recently conducted a course at the Harlem Valley State Hospital, Wingdale, N. Y., in the technic of this treatment for twenty-five physicians, who represented various New York state hospitals. The material consisted largely of patients with chronic states, having an average duration of about four years. In 2 cases, at most, the duration was possibly less than a year and a half. Some of the patients were mute and apathetic and others disturbed and under restraint; still others were able only to make stereotyped movements. Even with material of this type and in spite of the fact that there have been only twenty-five days of treatment, 8 patients are already fit for discharge, not with full but with social remissions; under favorable circumstances they can return to work.

An additional 4 patients will probably soon become eligible; so it can be said that though the treatment has produced no cures, it has at least proved its value. With 2 exceptions, all the remaining patients have improved sufficiently to adjust themselves to the requirements of institutional life.

#### CLINICAL EXPERIENCE WITH HYPOGLYCEMIC THERAPY OF THE PSYCHOSES. DR. BERNARD GLUECK.

I hesitate to report on the results of hypoglycemic therapy at this time because of the relatively brief period that has elapsed since the introduction of the treatment and, furthermore, because it has been difficult to resist the plea of relatives to employ this therapy for patients who have been ill for a longer period than is considered suitable for the treatment. Nevertheless, on the basis of experience with 19 patients, 11 of whom were schizophrenic, certain definite impressions have been gained which justify agreement with the opinion expressed by European authorities that hypoglycemic therapy offers a more promising approach to the problem of schizophrenia than anything hitherto available. Moreover, it raises important problems in connection with both the nature and the fixity of deterioration in schizophrenia and the nature and stability of the beneficial results obtained with this therapy. Indeed, the most characteristic and perhaps, from a practical point of view, the most important observation is the contrast between the unmistakably far-reaching beneficial effects of hypoglycemia on the psychotic state and the almost total lack of criteria it furnishes for predicting the degree of stability and permanence of improvement in the individual case.

The problem which requires most urgent attention is discovery of the real nature of the fixative that gives stability and permanence to the gains in patients who stay well in consequence of hypoglycemic therapy; what is the ratio of the constitutional, biochemical and psychobiologic factors?

All patients undergoing hypoglycemic therapy benefited to a greater or less extent from its unmistakable sedative effect. It is an impressive experience, indeed, to watch the diminishing need for sedative measures, chemical or physical, especially in patients who had required a considerable amount of sedatives before the treatment. The improved physical health, with the diminution of noisy, disturbed behavior, has an unmistakable effect on the general atmosphere of the hospital.

One notices, furthermore, improvement in the accessibility of the patients and the emergence of a capacity for transference, even in some who had been encapsulated in an autistic state for a long period.

To a greater or less extent, most patients have gained a better sense of and contact with reality. Orientation and interest in current events and in personal appearance improve regularly; patients who in some instances have had to have meals in their rooms for years are able to join others in the dining room. When one contrasts the behavior of these patients during the afternoon and evening with their manifestations during the hypoglycemic treatment, it is difficult to believe that one is dealing with the same persons. It is much more difficult

to generalize when one attempts to determine to what extent these changes in attitude and demeanor are paralleled by changes in the basic schizophrenic process. Certainly, the emergence of affability and friendliness and the capacity to cultivate transference relationships in persons who were previously wholly inaccessible must involve internal changes in libido economics, which go with modification in the hostility, aggressiveness and megalomanic tendencies of the schizophrenic patient, rendering less urgent the need for delusional, hallucinatory or compensatory defensive devices. Similarly, the diminution in shyness and fear which is associated with a freer and more natural contact with others must modify the need for withdrawal and isolation, perhaps even for regression in the psychoanalytic sense. In the absence of definite attempts at psychoanalytic ventilation and reconstruction, one must assume theoretically that the improvement which goes with hypoglycemic therapy consists in strengthening the forces of control and repression in unknown ways, so that they become more capable of dealing adequately with egodystonic, asocial and antisocial impulses.

As has been pointed out by every one who has written on the subject, and particularly by Sakel, the technic of hypoglycemic therapy does not lend itself readily to standardization of procedure. Each patient may call for a special adjustment of technic, and every day emphasizes the cardinal importance of experience. I have had to rely on my best judgment and that of my staff in meeting the various calls for adaptation of the technic to the requirements of the individual patient and in subordinating, whenever necessary, the claims of therapy to those of saving a life. For these modifications one naturally assumes full responsibility; it would lead nowhere at this time to discuss the bearings of these modifications on the therapeutic results in the individual case.

HYPOGLYCEMIC TREATMENT OF THE PSYCHOSES: EXPERIENCES AT THE BELLEVUE HOSPITAL. DR. JOSEPH WORTIS (by invitation).

What people wish to know is whether treatment with insulin can cure schizophrenia, or, if it does not, what can one expect from it? From experience at the Bellevue Hospital, I cannot yet answer these questions conclusively. Thirteen patients have been treated in the past four months, and the results stand as follows: The first patient with schizophrenia treated by Sakel's method was a man (J. J.), aged 30, whose psychosis had developed at least five years before. The case was described before the New York Society of Clinical Psychiatry on Nov. 12, 1936, after about eight weeks of treatment. All that could then be said was that the patient had shown striking, but transitory, remissions during treatment. The treatment has now been concluded; the end-result is negative.

Another patient with schizophrenia presented at that time is still receiving treatment. The improvement in this case was at first marked, but a relapse occurred, and the patient's condition is not much better than at the beginning of treatment. Improvement in the third patient, a young man with hebephrenia, was steady and progressive, in spite of the fact that the subject said that his mental changes started at least three years before. He is now without delusions and has full insight into his past psychosis, although he is still seclusive and has some hypochondriacal preoccupations. He says: "My thinking used to be mixed up. I must have been mentally sick. Now I can think more clearly, but I am not perfectly well yet." His manner is now more relaxed and friendly; he converses easily and says that he feels trustful and responsive, "like a child." He has been discharged as improved and is likely to make a satisfactory social adjustment.

In addition to these patients, my colleagues and I have treated 10 other schizophrenic subjects, most of them with recent illnesses; 3 already show full remissions, and others at the present stage of treatment show what could be called social remissions. Of the total of 13 patients I can say that 9 have definitely benefited from treatment and that 4 so far have not responded. We regard these results as positive. We believe that Sakel's hypoglycemic treatment has a beneficial effect on patients with schizophrenia and that it can induce full remission in suitable subjects. Whether our work will corroborate the results of Sakel and Max

Müller remains to be seen. Neither Sakel nor Müller has made extravagant claims; in 35 cases in which the duration of the disease was more than a year and a half, Müller reported only a single full remission, and Sakel has made it clear that his results in chronic schizophrenia leave much to be desired. We are satisfied to wait for further observation before the exact value of the treatment can be determined.

I shall describe some of our experiences in the management of hypoglycemic treatment. As a fairly typical example I shall take the first patient whom we discharged. An intelligent Negro boy aged 18 presented a picture of paranoid schizophrenia on admission. He said that strange things were going on about him, that persons on the street stared at him in a "funny" way and talked about him and that somebody had tried to poison him with a piece of candy. It all started six or eight weeks before he came to the hospital, and at the time of entrance he admitted that he was hearing voices that other persons did not hear and was seeing apparitions. He had always been a quiet, pleasant, studious boy, who adjusted well with this family and friends and had no big troubles or bad habits that he knew of. When I talked with him, he showed enough insight into his illness to deny his symptoms, but when closely and sympathetically questioned, he expressed them freely again. Dr. Karl Bowman, who examined him the day before treatment was started, declared that he expected that the patient would continue slowly to deteriorate and that he would never return to his previous prepsychotic level.

Physical examination gave normal findings. On the day following Dr. Bowman's examination the patient was given the first injection of 10 units of insulin, which was followed by four hours of hypoglycemia. The dose was increased to 15 units the next time and to 20 units on the following day. The patient showed no particular response and continued to be quiet and seclusive; he smiled to himself at times and said, when questioned, that he felt "kind of low."

When spoken to during hypoglycemia, he said that he felt shaky and hungry and that his heart was pounding. "I don't think that I am going to like these treatments," he said. When questioned further, he said: "I don't notice any difference in my feelings." When he was given sugar water, he complained of headache, lay back in bed, pulled the covers over his head and fell asleep. He reacted to 20 units of insulin with mild perspiration, rapid pulse and somnolence. When he was asked how he felt about the treatment at this time, he said: "After I get the injections, I feel a little bit better; but my hands tremble, and my voice trembles, too."

On the following days, with gradually increasing doses of insulin, the patient began to show improvement but was still uncommunicative and seclusive and rather evasive when questioned. On the tenth day of treatment, after injection of 40 units of insulin at 8 a. m., the patient showed his first marked hypoglycemic reaction: About three hours after the injection he stared fixedly ahead and began to salivate and show twitchings of the muscles of the mouth. Half an hour later he cried out suddenly and had a typical epileptic seizure with tonic spasms, biting the tongue and stertorous respiration. Both the hypoglycemia and the seizure were quickly relieved by intravenous administration of dextrose. The patient was depressed and complained of headache but slept well for several hours thereafter. The patient's improvement next day was marked. He was cheerful and communicative throughout the day. "I know I had a lot of silly ideas," he said, "but they're all gone now." Treatment was resumed, and on the seventeenth day of treatment the patient went into coma for the first time, after an injection of 50 units of insulin. Only a few more daily shock reactions with deep coma were necessary. On the nineteenth day of treatment the patient was free from symptoms, both in and out of hypoglycemia. He showed full insight into his past delusions and hallucinations and said he felt like his old self again.

The dose was thereon dropped to 30 units of insulin and the hypoglycemic period limited to two or three hours on the following days. The patient was cheerful, friendly and responsive; he played games, conversed freely, smiled readily and slept well. He had gained 17 pounds (7.7 Kg.) during treatment.

When he was questioned by Dr. Bowman on the day before his discharge, the patient gave the following account of his illness: "I began to have a strange sick feeling about a month and a half, or two months, before I entered the hospital and had to stop work a week before I came here. It seemed as if people were looking at me; very little noise would irritate me—I even told my brother one day I thought people were following me. It was just my imagination—some mental illness I had—and all the time I wasn't aware of it. That's why I never complained. When I went to bed at night, it seemed like I heard voices. I remember one night I went into the lavatory to cut off the water dripping into the tub—seemed like I could hear voices coming out of the water. Gradually it got from bad to worse." (What did the voices say to you?) "It was like accusing me. It said that I'm a thief and that I don't love my family—and ideas along that trend." (Before you received the first injection, were you still hearing these voices at all?) "Yes, I was. I couldn't do a thing. Couldn't concentrate. I know that if I was reading a book, I wasn't actually reading the book—I was listening for something else. But I always said that I was well because I wanted to leave the hospital. About three weeks ago the voices stopped, and now I feel just like myself. I don't feel confused. No, I don't feel afraid. I used to feel uncertain; I don't know what made me have that feeling; now I feel all right, like my old self."

Dr. Bowman's final note stated, in part: "My judgment in this case is that there has been definite and marked improvement immediately after insulin treatment and that this treatment has been an essential factor in the production of the remission. . . . There appears to be essentially a complete remission, but only after years of observation would one be in any position to claim that the remission is permanent and that there is anything like a complete cure."

To sum up our experience with this patient: We relieved all the symptoms of a young man with schizophrenia of recent onset with four weeks of insulin treatment with hypoglycemia. Improvement started after a few days of treatment, before shock doses were reached. The patient's response was at first fluctuating and uncertain, and he had most relief during the hypoglycemic period. He showed the most marked improvement after an epileptic seizure and became emotionally stable, with full insight into his past illness, after a few days of deep insulin shock with coma. The highest dose of insulin needed was 60 units, and the entire treatment lasted four weeks.

There are several points of special interest in this case. First, the course of treatment was relatively short; most patients need six weeks or longer before they show a stable response. Second, the improvement started before high doses of insulin were used and before actual shock was produced; moreover, the patient passed into deep coma only three or four times. Finally, the patient showed the reversal of reaction first described by Sakel, that is, relief from symptoms during hypoglycemia at an early stage of treatment, with reactivation of symptoms during hypoglycemia at a later stage. Sakel has declared that treatment should ordinarily not be concluded until the patient is free from symptoms both during hypoglycemia and thereafter. This patient continued to show occasional transitory psychotic symptoms during hypoglycemia in the final phase of treatment; he told me that a few of his old ideas came back for a little while after the injection. However, he had already been told that he was to go home in a few days, and we did not wish to disappoint him. This may have been a mistake. His attitude on the whole was solid and sure enough to warrant discharge, but he had been more robust and outgoing during the preceding week. A month has passed. The patient is observed every week and continues to be well; if he should become psychotic again, we shall profit from experience and treat him more thoroughly next time.

If any mistake was made in the management of this patient, it was on the side of undertreatment. However, one can make mistakes in the opposite direction. Another patient with schizophrenia seemed to have reacted poorly because of overtreatment. A boy whose first symptoms had developed six months before he came to the hospital showed marked apathy, tenseness and restlessness on admission and acknowledged having delusions and hallucinations. He showed

marked improvement after three weeks of treatment with doses of about 150 units of insulin. He became amiable, cheerful and responsive; he was free from delusions and hallucinations and had apparent insight into his past illness. At this point, however, he spoiled his hypoglycemic response one morning by stealing and eating food before he could be stopped. He was in an indifferent state that day, and the doses were increased thereafter. Soon he began to complain that he was receiving too much treatment and insisted that he was well enough to go home. The doses were increased to over 200 units and then dropped to 100 units, without success, and the patient showed a marked relapse. It seems probable to me, though I cannot prove it, that more cautious management of the dosage, with days of rest interpolated at the right time and proper psychotherapy and occupational therapy, might have prevented this result. My belief is that the results were spoiled by overtreatment.

It is often difficult to know when to conclude treatment. A young man who was admitted to the hospital with symptoms of paranoid schizophrenia was sufficiently improved in a short time without treatment to cover up his symptoms successfully, so that they were elicited only by close, careful examination. When treatment started, he showed marked reactions to relatively small doses of insulin and exhibited florid psychotic symptoms during hypoglycemia. It could be seen that the patient's psychosis was not far from consciousness and was ready to reappear with relatively slight provocation. In spite of the fact that the patient was sometimes free from symptoms we continued treatment steadily with high doses and deep coma and found, to our satisfaction, that he was growing less evasive and more confiding as the hypoglycemic symptoms disappeared. It was as if the recent delusions had been submerged only a little way and no solid barrier had yet been formed between the latent psychosis and the conscious thoughts. We shall continue to treat this patient until he becomes free from symptoms during hypoglycemia.

Almost regularly in the course of treatment one sees a stage of improvement at which the patient is free from symptoms but susceptible to suggestion and is only too ready to retreat again to the delusions he has just abandoned. When this point is reached, one must proceed cautiously and avoid close questioning. The patient is in the position of a person who has awakened from a disturbing dream of particular intensity and requires some activity of normal waking life before he can be free from its influence. He wants to repress and forget. Deep psychotherapy is contraindicated, and insulin treatment must continue. One might compare the psychosis to a suppurative process which has to be localized and encapsulated before it can be drained.

How much insulin must be given to produce coma? That varies. Occasionally a patient will pass into coma with 40 units or less, and the patient in the bed beside him may be receiving 200 units to which he responds with exhausting excitement but without coma. Coma may develop in this patient with 230 units, and when the dose is suddenly dropped to 150 units he may pass into still deeper coma. At a later stage of treatment he may respond to 80 units with deep coma. I do not know why this is so. I can conclude only that some general tendencies are involved: (1) Chronic conditions are often more resistant to insulin than those of recent origin; (2) sensitivity to insulin increases as the treatment progresses, and (3) improvement in the patient's mental state is often associated with increased sensitivity to insulin.

Dr. D. Ewen Cameron tells me that a relapse in the patient's mental state is associated with increased resistance to insulin. This accords with Dr. Sakel's experiences and our own.

The reactions of our patients to hypoglycemia generally run true to type; any one patient may repeat the same series of reactions during hypoglycemia every day in about the same order. One patient, for example, at an early stage of treatment went through a period of excitement every day, marked by a particularly low order of phonation. He made crude guttural sounds or bellowed or screeched like an animal. As treatment progressed, the excitement was marked instead by a special low order of mastication. He ground his teeth and bit and

gnawed apart the bedding. On being aroused from coma, he was always surprised to find a wad of brown cotton or wool of about the same color as the blanket lodged in his mouth.

Another patient almost regularly showed more or less generalized myoclonic twichings in about the third or the fourth hour of hypoglycemia, usually of sufficient severity to warrant termination of the hypoglycemia by tube feeding. We decided one day, however, to permit these myoclonic seizures to continue while we watched the patient. In half an hour the twichings had ceased, and the patient went into deep and quiet coma, with flushed face and profuse perspiration, and showed definite improvement thereafter. It seems justifiable to talk of reaction types, though the types are by no means stable but are liable to undergo gradual, or even sudden, change with treatment. There seems in general to be a tendency for a mild reaction to be associated with benign conditions or with states that are beginning to respond to treatment.

The patients up to the present have shown no untoward physical effects of treatment. On the contrary, almost all say that they feel better and stronger. They put on weight; the color improves, and in several cases I have noticed that lesions of facial acne clear up quickly. None of our patients has yet been in serious danger—thanks largely to the precautions we have learned to exercise from Sakel's experience. The special technic of tube feeding which he devised, the rules for management of the hypoglycemic state, the special precautions following termination and the close observation throughout the day and night for late shock have so far prevented any mishaps, though it is probable that in any large series of cases, even under skilled management, an element of danger will remain. The behavior of the heart during treatment has been the subject of special studies by de Châtel and Palisa (*Klin. Wchnschr.* **14**:1784, 1935), in Vienna; Hadorn (*Schweiz. med. Wchnschr.* **66**:936, 1936), in Switzerland, and Giauni (*Clin. med. ital.* **67**:309, 1936), in Italy. Sustained tachycardia frequently developed in the course of treatment. Sakel recommended the free use of digitalis prophylactically. In 2 of our cases of tachycardia there was prompt relief with digitalis. Since opinions vary, however, on the prophylactic value of this drug, special work will be needed to clear up that point.

Five of our 13 patients had epileptic seizures during the course of treatment—of whom 4 had only one attack and 1 several. This corresponds with Müller's observation that one third of his patients had epileptic seizures at some time during the course of treatment. When seizures occur, we give intravenous injections of dextrose, but some observers believe that these hypoglycemic seizures are not only harmless but beneficial to the patients. In 2 of our cases we noticed marked improvement after the seizures, and in no case did we observe any relapse in the patient's mental state. Sakel recognized the possible benefits of these seizures but compared them with heavy artillery and expressed the opinion that one ought to work with the infantry if possible.

This work will afford a rich opportunity for further physiologic observation in the fields of neurology and metabolism. Two of our patients, for example, cannot be aroused from coma by feeding by tube quantities of a solution of cane sugar, even though we wait half an hour. After twenty minutes the blood sugar levels are still below 60 mg.; both patients are aroused promptly by intravenous administration of dextrose. Since in both cases there was evidence of normal absorption of sugar from the digestive tract before treatment—as indicated, at least, by the curves for sugar tolerance—it may well be, as Dr. L. L. Orenstein has suggested, that the sugar is trapped in the hungry liver before it can reach the larger circulation. Or it may be, as Dr. E. W. Lazell has suggested, that these subjects cannot properly utilize cane sugar.

Another point of interest is the compensatory reaction of the endocrine antagonists of insulin, particularly epinephrine. Certain symptoms of hypoglycemia—dilated pupils, rapid pulse and tremulousness—seem to be due not to insulin as such but to the compensatory secretion of epinephrine which it provokes. Cannon and his associates (*Am. J. Physiol.* **69**:46, 1924) were the first to demonstrate experimentally the compensatory secretion of epinephrine in hypoglycemia, and other authors have confirmed this work—more recently, Brandt and Katz (*Ztschr.*

*f. klin. Med.* **123**:23, 1933), in Germany. I have been particularly interested in the relation of hypoglycemic excitement to epinephrinemia. In 1 of our patients (J. J.) rather marked excitement developed after about three hours of hypoglycemia, but he became particularly lucid thereafter. I wondered whether the excitement might not have some useful function in preserving homeostasis in the patient—perhaps, I thought, it is not due to excessive production of epinephrine but is an effort to provoke the secretion of epinephrine so that the stores of glycogen can be mobilized. If this is so, injection of epinephrine ought to have a sedative effect. We tried it, and it did. Hypodermic administration of 1 cc. of a standard solution of epinephrine hydrochloride during hypoglycemic excitement produced complete pacification of 2 patients in a few minutes. It is reasonable to regard the motor excitement in hypoglycemia as an effort to compensate for depleted stores of epinephrine or to release carbohydrate stores without the help of epinephrine. Dr. Paul Hoch, of the Manhattan State Hospital, told me that he has pacified catatonic excited patients with epinephrine in the same way. Perhaps psychotic excitement, like fever, has, after all, a useful function.

These problems arise as our work goes on. We can afford to wait for further results and observations, but in the meantime we have every reason to welcome an important and invigorating new influence in psychiatry.

#### DISCUSSION

DR. CLARENCE O. CHENEY, White Plains, N. Y.: It will be recalled that a long time ago it was advocated that patients could be benefited materially by being brought as near death as possible by the use of opium; that was tried for a number of years in many of the older hospitals. I do not know why it was discontinued. Another method, described as early as 1854 by Dr. Isaac Ray, superintendent of the Butler State Hospital, Providence, R. I., was that of etherization of patients. As one reads the literature, it is apparent that there was at that time a great deal of discussion and difference of opinion about the efficacy of this form of treatment. The effects of etherization of patients, as one reads of them, were much the same as those of hypoglycemia today. At first, apparently, a great deal was claimed for it. It was presumed by some persons to be a cure-all for mental disorders. The truth prevailed eventually, and it was used less and less. As far as I know, ether is not used at present in treatment for dementia praecox or other mental disorders.

In discussing the present form of therapy, one has to keep in mind that one is treating not a specific disease entity but persons who have tried to meet certain situations and whom one is attempting to train to meet situations differently in the future. If, as Dr. Sakel and Dr. Glueck have emphasized, the psychologic features and implications are important in this treatment, as they are in most psychiatric therapy, one will not be surprised if some physicians obtain different results with some patients than other physicians secure with others. I think all are agreed that before one can draw final conclusions about the efficacy of this treatment, one must first have reports on a large number of patients observed over a fairly long period; I think, also, that because of the psychologic factors in both the physician and the patient which must be considered, one should not be surprised if in the future one secures divergent reports from different sources, so that it will take a long time to reach a conclusion satisfactory to every one. Complete control of the experiment is not at hand. There are too many variables, as there are in most experiments with human subjects, to permit one's drawing a quick and final conclusion. It would be tragic if eventually the enthusiastic reports that have come from Europe are not corroborated in this country—tragic for those whose hopes have undoubtedly been raised to a high level. It may be said already that hypoglycemia is a method of treatment that can change certain patients, as Dr. Glueck has stated. It is not yet known how these changes are carried out or what the mechanism is. A great many things cause changes in patients with dementia praecox, but I hope this treatment may continue to prove an instrument for alleviation of this distressing disease.

DR. KARL M. BOWMAN (by invitation): Those who have been in psychiatric practice for some time will remember that Kraepelin advanced the theory that

dementia praecox may be due to a metabolic disorder of endocrine (thyroid and gonad) origin; so the possibility of endocrine factors in dementia praecox or schizophrenic conditions has been recognized many years. Many have tried, rather unsuccessfully, to alleviate this condition with various types of endocrine treatment—feeding of everything from the pineal gland to the gonads. Most have disregarded the idea that the pancreas, a gland of internal secretion, may be related to schizophrenia, and therefore, in spite of the large number of endocrine studies and attempts at treatment, this possibility seems to have been almost neglected. All are grateful to Dr. Sakel for pointing out the importance of the pancreas and its secretion and the effects possible from its use.

The point should be made that the therapy is not to be compared with ordinary treatment with drugs. Every speaker so far has emphasized that point. It is not comparable with giving arsphenamine in syphilis or even with the malarial treatment for dementia paralytica. It is a much more complicated procedure, with many unknown physiologic and psychologic factors entering into the equation. After many years of work Dr. Sakel has perfected a technic, although in some of his procedures he remains at a level at which, he says, he acts without quite understanding why he does so, since experience has taught him it is the thing to do. If, with his experience, Dr. Sakel still has to treat patients in that fashion, there should be a word of warning against the indiscriminate use of insulin in the treatment of schizophrenia by persons who are unfamiliar with the procedure and who have no experience with all the complications that may develop. Dr. Sakel has pointed out that the value of the treatment may depend as much on the proper termination of the hypoglycemic shock as on anything else. That is certainly one of the most important factors, and if one tries to find out just when to terminate the hypoglycemic condition, one finds that it is not something that can be written down in simple terms and passed on to some one else. One may expect, therefore, that, as Dr. Cheney has emphasized, there will be variable results from this treatment and that one reason will be that some physicians will not use the same technic which Dr. Sakel employs. If one is to think in terms of Dr. Sakel's method and his results, it is important that this distinction be kept clearly in mind, for it is not fair to judge the Sakel method by results, either better or worse, which may be obtained by persons who are not using his exact technic.

One should also emphasize, as Dr. Sakel has said, that the therapeutic effects do not depend on the amount of insulin used or the duration or depth of coma. As I said before, they depend more on the accurately timed moment of interruption of the hypoglycemic state. The blood sugar drops to a very low level with small amounts of insulin, and it does not drop any lower when one gives larger doses of insulin. This indicates that not merely the amount of hypoglycemia determines the effect. Dr. Sakel has pointed out also that what he calls the wet shock produces in most cases a more beneficial result than the so-called dry shock. Here, again, one finds that there are patients who do well with the dry shock. In other words, the subject is still confused, at least to most persons.

Dr. Sakel has indicated also that the term "shock" is a misnomer, and, as Dr. Wortis found in a case which he reported in some detail, a patient who had little shock or coma in the treatment responded excellently. The so-called shock treatment with insulin is not comparable with the type of shock in bringing a patient as close to death as possible, which Dr. Cheney mentioned. It is not simply a shock of that sort which accomplishes the result. It is something else—I do not know what—but, in my opinion, something rather different.

One should emphasize what Dr. Sakel has said of the four phases of treatment—the preparatory phase, the phase of shock, the period of rest and the polarization or terminal phase. Polarization, which Dr. Sakel has described this evening, is most interesting. When one watches, one sees the manner in which the psychosis disappears in the state of shock and later reverses itself; finally, the patient becomes free in both phases. It is a specific reaction.

I have been struck in a number of cases at the Bellevue Hospital by the apparently prompt disappearance of hallucinations and the appearance of insight,

before the patient seemed to be otherwise much improved. That has been mentioned also, but it has been to me one of the outstanding things noticed early in treatment. It seems almost specific in relation to this type of treatment.

DR. JOHN ROBERT Ross, Wingdale, N. Y. (by invitation): Possibly a brief statement relative to the hypoglycemic treatment now being carried on at the Harlem Valley State Hospital under Dr. Sakel's personal direction will not be out of place. Dr. F. W. Parsons, commissioner of the New York State Department of Mental Hygiene, expressed the belief that if this treatment has merit it should be made available for the great group of patients who fill the state hospitals but that before all the institutions embark on this course, it should be tried out at one of them and physicians should be sent for instruction in the technic from Dr. Sakel himself. The Harlem Valley State Hospital was selected for this purpose. The treatment has been going on for five weeks.

It was decided to treat 20 patients. Forty patients were selected from the institution who were thought to be representative of those admitted to the hospitals with early stages of the disease. Of these 40 patients I obtained permission from the relatives for the treatment of only 20, so that the criterion for the selection of patients was the permission of the relatives. The best patients were not secured, by any means. I could not give a favorable prognosis for any patient I presented to Dr. Sakel.

I have watched the treatment from the start. There is not a shadow of doubt in my mind that there has been definite improvement in a number of cases and considerable improvement in others, while in 2 instances I doubt whether there has been any change. I am not prepared to say that any of the patients has recovered, but a number have improved to such an extent that they will be sent home for trial. It is only after they have had observation outside, under the stresses they will meet in the world, that one can draw conclusions as to whether there is even social recovery. If this treatment offers a chance to bring about even social recovery in a sufficient number of persons in the state hospitals, the economic value to the state of New York will be considerable.

A criticism I have heard expressed by physicians who are receiving instruction at the hospital and by some outside concerns the time at which the hypoglycemic reaction should be stopped. If one is asked how one determines the right time at which to remove a patient from the state of hypoglycemia the question is difficult to answer. Unfortunately, the word "intuition" has been used. It is ill chosen. That is not what is meant. From my observations and from my talks with Dr. Sakel, I am convinced that experience and judgment are meant. No one can define experience in definite terms. It is something which one must obtain by observation and study, and it is hoped the men who have been taking the course are getting some of this experience.

It is too soon to make a definite statement about the type of patients. Until many more patients have been treated in state hospitals and considerable time has passed for observation, one is not in a position to say definitely whether it is going to have as much value as one hopes.

Men from all the state hospitals have now received a course of instruction under Dr. Sakel. I think they understand his technic fairly well. When they return to their institutions, I believe it is reasonably safe for them to treat patients, without causing deaths. Whether they are yet competent and have the experience to bring about the best results in their patients I do not know. My associates and I feel reasonably encouraged to go on with the treatment. We hope we shall be able to gather statistics that have value and, above all, that we shall have the cooperation of the outside physician who sees these patients first, so that they may be sent at an earlier stage of the psychosis than heretofore. In all our cases the duration of the psychosis was never less than one year, and in 1 instance it was thirteen years. Our patients were not particularly good material, but we are reasonably encouraged to think that a social recovery, at least, may be brought about in some of them.

DR. D. EWEN CAMERON, Worcester, Mass. (by invitation): It is of practical importance to discuss Dr. Glueck's findings with private patients in the light

of those which my colleagues and I obtained at the Worcester State Hospital. I gather that the patients coming to Dr. Glueck's hospital have earlier stages of the disease and are better able to afford special nursing facilities. Our material is representative of the usual run of patients admitted to state hospitals. I believe that if this method is to establish itself, it must do so as a means of treating a group which represents immeasurably the greater proportion of schizophrenic patients entering the hospitals, namely, those admitted for the first time to the state hospitals.

Dr. R. G. Hoskins and I have been investigating the insulin treatment of schizophrenia at the Worcester State Hospital for nine or ten months; during that period we have treated in all 15 patients. From the reports from other centers and from our own earlier investigations, it is apparent that experience and the utilization of very early stages are important factors. Without these, it would seem that it is impossible to equal the results reported from Vienna, Switzerland and, more recently, from Zagreb, Jugo-Slavia. Consequently, since experience had to be acquired and since patients with very early stages were, and still are, hard to secure, we set as our objective the question whether insulin produces ameliorative changes of any kind, leaving to a later date the problem of what percentage of favorable results can be obtained.

Our findings have demonstrated that insulin produces amelioration in the majority of cases. These changes, for the most part, are more favorable the more recent the condition. The first changes appear to implicate the quantity of behavior. Patients who show overactivity and impulsiveness become quieter. Patients who show dulness and retardedness tend to become more responsive and active. At the same time, rapport is improved. The patient is often more approachable and seeks to orient himself in his social milieu. Later, delusional and hallucinatory activity becomes less vivid and seems to mean less to the patient. He talks of it less, and later it may be found that it no longer exists, though the patient may have no insight into his past experiences. Finally, in favorable states insight is attained. Possibly the most marked change is in the field of concentration. Patients who have been incapable of reading or of centering attention on a topic of conversation for any length of time often show definite improvement in this regard. Finally, we have noticed that patients who had early shown no overt sex interests, or purely auto-erotic interests, began to exhibit definite development of heterosexual activities. On the other hand, we have found that relapses occur frequently and that in some cases in which favorable progress was made initially, a plateau seems to be reached beyond which it is difficult to press the patient. It is necessary to add, however, that these experiences become, or seem to become, less frequent the more experience the worker acquires.

From the first, we have occupied ourselves with what seemed to be the two major questions which must be answered if the method is to prove of value. First, is the improvement which this method produces greater on the average than might be expected from the rates of spontaneous remission, and, second, is the improvement greater than would be expected from the extra care and attention given to patients undergoing this treatment? In answering the first question, it is important to keep in mind that the rates of remission reported in the literature referred to the number of remissions occurring within a fairly extensive period, usually from one to five years, but that the improvement which follows insulin treatment appears from within a few days to a month after the beginning of treatment. In other words, the probability that treatment and improvement are related causally is great indeed. In answering the second question, namely, whether the extra care and attention might not be a major factor, it is to be noted that among our patients with early stages of the disease were several in whom experimental procedures involving much work by the staff had been carried out without amelioration in any way comparable with that following insulin treatment. Moreover, all our patients were given a detailed daily examination in the psychologic and biochemical laboratories for a month before treatment, again without any amelioration. Finally, 3 of our patients were sent for a holiday of three or four

days during the course of treatment. Though they were much more the center of interest and attention at home than they had been at the hospital, 2 came back with minor relapses.

We have been particularly interested in the phenomena of relapse and believe that a certain constellation of symptoms is associated with it. In our restricted experience, patients who are improving show increased sensitivity to insulin, an increase in weight and a possible rise in the basal metabolic rate, as well as the mental changes which I have already mentioned. Patients who are in relapse require more insulin to produce the same symptoms. Commonly, during relapse there are a fall in weight and, again, a questionable decrease in the basal metabolic rate; the patients become less interested in their social milieu and show in greater or less degree a return of the former symptoms.

A further factor which runs concurrently with these changes and which may prove to be of value is the pattern of the brain waves. Records were made by Dr. G. Hoagland and Dr. H. H. Rubin in a study of our patients at the Worcester State Hospital. In the schizophrenic patient the variability in the records of brain waves is much greater than in those of the normal subject. As clinical improvement takes place, we have found that the variability becomes progressively less and that in patients that have returned to normal or near normal the variability also returns to or approximates the normal. On the other hand, when relapse occurs, the variability increases. Though more confirmation is required, the relationship gives promise of being close.

DR. SMITH ELY JELLIFFE: I find myself in an ambivalent position: embarrassed in that, unlike my predecessors this evening, I have as yet never seen a patient during or after hypoglycemic treatment with insulin and emboldened in that this ignorance of the actual clinical picture permits me to start with another type of observation derived from extensive preoccupation with the literature. I have seen several hundred cases through the eyes of their respective reporters. What I have reconstructed of these kaleidoscopic pictures comports closely with the material presented this evening. This reconstruction emphasizes the enormous diversity of the clinical reaction types and threatens to defy all efforts to bring order into the phenomena. Yet one cannot escape the desire to see order in the reactions and to bring this diversity into correlation with the nucleus of the schizophrenic process.

One of the speculations concerning the apparent disorderly diversity of reactions is associated with the schizophrenic patient; no two are ever quite alike, yet all have a certain generic resemblance, more particularly in the Bleuler codification. To an observer steaming up the Hudson, the sky-line of lower New York as seen on a misty day presents an amazingly varying picture every hundred feet or so. Certain high points become obscured, and others take their place. This shifting panorama, so varied as to defy description, is a crude metaphoric parallel to the infinitely greater kaleidoscopic imagery of the schizophrenic motley.

From the standpoint of a phyletic psychopathology concerned with the different id impulses of each of the libidinally invested organs of the body, it is no wonder that the clinical pictures, roughly grouped as a schizophrenia, are infinitely varied as to aspects of fixation, regression and cathexis, at various levels of psychobiologic evolution. Also, to recall the metaphor, it is not incomprehensible that, both in the libidinal and in the destructive aspects, the functional evolution of certain organs such as muscles and the respiratory, oral, anal and genital organs, should stand out like the more conspicuous buildings of the landscape.

From this point of view, which I deem important, it is little wonder that the so-called activated psychoses of hypoglycemic shock should be variable. There is, however, I believe, no activated psychosis; rather, one sees various clinical pictures of regression to primitive, infantile behavior of a type approaching the fundamentally normal aspect of very early intra-uterine life, or to higher stages of behavior. Here the death threat by the withdrawal of glycogen forces definite withdrawal of libido from the aggressive, hostile, anal, oral and other negativistic behavior patterns. Coma, to say nothing of its antecedent, less regressive phases, brings the subject practically into an intra-uterine bath of primary narcissistic

omnipotence. By the hypoglycemic threat one can envisage a type of phylogenetic dissection by a metabolic tool from the frontal forebrain back to the medullary respiratory and vagal nuclei and a decerebration experiment of a subtle form by a pharmacodynamic type of instrumentation.

This onslaught by the death impulse, with its consequent alteration of autistic, negativistic, hostile behavior, has been noted for centuries, even if not phrased in this peculiar form. Even in the days of early Greek medicine it was noted how a severe so-called somatic disease process often cleared up a peculiar bit of social behavior. Typhoid, influenzas and pneumonias occurring in psychotic persons have been known from remote periods to be followed at times by recovery from the distorted social behavior. The tenons of the Chinese that kept up an open sore in the neck are an early example of the empirical treatment which, as one skips the centuries for lack of time, reemerged in the injections of *Bacillus pyocyanus* by Wagner von Jauregg in Vienna, as early as the 1880's. Then came anaphylactic shock reactions and efforts to secure *Dauernarkosen*—strangely similar to later developments. Schuster's work in 1926 may be taken as an example, as well as his early efforts with insulin, not unlike those of Sakel.

None of these studies—and one could spend an evening reciting them—deserves as much attention as the refinements of the Sakel procedure. Here is something impressive, made doubly so by the increased weight of the Freudian libido hypothesis as it pertains to the psychic dynamics of schizophrenic behavior.

As the preceding speakers have all been wary with reference to prophecy, so shall I be with regard to the process of libido economics as pertaining to theories of explanation. Here a great deal is to be said, which, when compressed within the crude formula of withdrawal of the libido from the outside world and its fusion with the death impulse for the maintenance of the narcissistic ego, is a mere gesture at understanding. Again, one sees complete release from the more superficial layers of the tyranny of the superego. The world becomes a loving, not a threatening, world, and early erogenous zones are permitted a certain freedom of functioning. Hence, it follows that a judicious form of psychotherapy can be, it seems to me, of great value in synthesizing a fragmented ego, which heretofore has been powerless against the onslaughts of the id and the tyranny of the superego. Here are great opportunities for psychopathology.

It is not without importance to emphasize the obvious, but rarely considered, idea that death is as complicated a process as life. Phyletically it has gone through a number of stages; just as the book of life has many pages, so has that of its rival, death. Thus, the death threat may vary enormously in its significance and demands on libido economic distribution. There are innumerable death threats from without that entail increased investments of object libido and many threats from within. The hypoglycemic death threat, however, is unique. Genetically, it may be thought of as a primordial, primitive and massive threat, which strikes at the initial stages of life's upholding. When it is recalled that, even before primitive life appeared on the earth, primitive carbohydrates were formed by the action of ultraviolet light on carbon dioxide, water and ammonia, it requires no great biochemical insight to realize that carbohydrates were among the first energy-transforming substances which created life. The stages of this upbuilding will not be rehearsed here, but emphasis on the utilization of carbohydrates in muscle-nerve functioning has a long phyletic history; hence, the death threat is more vital when coming from this direction than from almost any other. This thought, which could be expanded a thousandfold, is of no small significance in the startling and dramatic clinical pictures which are seen in insulin therapy for schizophrenia.

As to the problem of holding the remission, a suggestion consists in the employment of a less direct and virulent attack on the body by the use of ordinary insulin or by a combination of it with a slower and more gradually acting insulin. Such is protamine insulin, which, after the initial destruction of the set-up by insulin proper, can, by prolonged and judicious use, keep the patient in just sub-minimal balance on the edge of the death threat. This should be just sufficient to

keep the libido from active excursions into forbidden fields and to permit the synthesis of the ego and the relaxation of the superego which are among the goals of psychoanalytic psychotherapy.

I should like to say a great deal more about hostility (fight), the biochemical behavior of the adrenals, liver and muscle-nerve apparatus and the mobilization of glycogen and its destruction, as well as the myocardial situation which is related here; the hour is late, however, and others know more about these problems than I. I have thrown enough into the arena for many hours of discussion.

One more comment in line with another issue pertains to the possibilities of danger and rests on experimental work on hypoglycemic poisoning and tissue changes. Schmid's work (*Schweiz. med. Wochenschr.* **66**:960, 1936) here is most recent; briefly, it showed that the pathologic reaction in hypoglycemic poisoning with insulin lies within the zone of reversible tissue changes. This is encouraging so far as the danger lines are concerned and adds further zest to this promising new therapeutic adventure.

DR. ADOLF MEYER, Baltimore (by invitation): The society has had an interesting and informative account, presented by the ingenious originator, an enthusiastic follower and a conscientious worker, of something that has not happened often in the realm of psychiatry—the introduction as therapy of what had become known as a complication and hazard in the treatment of another serious disease, diabetes. It is particularly interesting because of the sharply time-limited production of a profoundly stirring, temporary and remarkably controllable dissolution of the patient in what figures in the mind and experience of most psychiatrists as a long-drawn-out, fateful disorganization. There are psychiatrists who regret perhaps that one speaks of "the treatment of schizophrenia," which one would like to meet on its own ground, in that self-absorbed, discordant reaction in which the patient is no longer in adequate constructive contact with his own nature, with reality and with the physician and in which the physician finds himself more or less unable to penetrate a vicious circle that spells frustration. One is confronted with a state which may be described in many ways—either in the highly interpretative language of Dr. Jelliffe or in the language of much simpler description of fact and evaluation of fact—and which so far has been treated by understanding, reorientation, occupation therapy and redirection of the patient's resources. The somewhat analogous empirical, but directly justified, fever treatment for dementia paralytica has taught that even in the clearly structural reaction to spirochetal invasion one should not attach the pessimistic note of irreversibility to the early diagnostic signs of defect in memory and judgment because they become irreversible at the end. G. Stanley Hall facetiously said that if schizophrenia should be called dementia praecox from the start because of what is frequently the end, Kraepelin should have called dementia paralytica "dementia thanatica," i. e., "deadly dementia," which, however, today it no longer is. There are psychiatrists who do not see in schizophrenia a fatal, irrevocable and final shutting-off of the patient and the physician from corrective and curative resources as long as one is uncertain of the existence of any specific lesion and the primary, or merely incidental, nature of what may be observed. One may hope that Kraepelin overreached himself with his diagnostic-prognostic ambitions in this field as much as with the same principles in his notoriously overfrequent diagnosis of dementia paralytica (see his record, *Psychiatrie: Ein Lehrbuch für Studierende und Aerzte*, ed. 8, Leipzig, J. A. Barth, 1909, vol. 1, p. 527; ed. 9, 1927, vol. 1, p. 759). The number of cases in which the physician is uncertain whether one should pin the discouraging and frustrating note of dementia praecox to schizophrenia has long been known to be sufficiently great to justify one in considering even distressing and forbidding features as not necessarily final or beyond the resources of further study and attack at the root. Dr. Sakel introduces an attempt to break through the apparently indestructible obstacle in a way that may be helpful on the basis of more than one principle. One might think of insulin as a "drug" that, even from the beginning of its use, proves to be a

stimulant with a relatively favorable effect on the arousal of sound appetites, even without the shock; on the other hand, one sees also how the complete reaction with the shock experience may insert itself in an exceedingly profound and interesting way, breaking up the variously deep frustrating states in what is called schizophrenia. At any rate, one is led to hope that here one can apply an effective immediate measure through short-timed, but repeated, reactions in the more prolonged, usually resistive process or reaction—a reaction capable of attaining an unprecedented number of remissions. These reactions to insulin are remarkable through the fact that a patient can be brought close to dissolution and risk even of death in the forenoon and in the afternoon can go about actually feeling better, owing either to something in the nature of the reaction to insulin or to certain fundamental changes in a condition that one never would have expected to reach with such rapidity by means of the usual methods of reorientation and occupational procedures, which do not permit such a deep therapeutic attack on the person. If favorable results ensue, it will become necessary to determine what one is working with, for it is obvious from the statements of Dr. Sakel and the other speakers this evening that they insert into a relatively complex disease situation another equally complex therapeutic situation with an as yet almost unpredictable variability of reaction. One is no doubt still confronted with something that has definite dangers. Fortunately, the reaction is remarkably reversible and controllable. From profound coma the patient can emerge in a happy mood and in two hours be capable of occupying himself and eating his meal in a way that surpasses anything known with any other pharmacologic or biologic effect. But these things have to be studied under proper conditions and under the direction of competent investigators. The procedure ought not to be foisted on the public as something already settled and to be tried at random by those who do not know much or anything of what schizophrenia represents or much or enough of what one can run into with the insulin attack. I believe that the medical profession owes it to the public and to itself to see that these studies are made under conditions which can give a well recorded account of themselves. It is therefore to be welcomed that the state of New York has taken the precautions to make sure that the experimentation is not made by untrained persons. Shortly after publication of the accounts, which undoubtedly had raised excessive hopes in innumerable persons, there came a flood of letters appealing for immediate application of a panacea. I am convinced that the careful study of this problem in qualified centers and under qualified instruction presents the only way in which the medical profession can do justice to the patients, to the public and to itself. Fortunately, this is made possible in an extensive way by virtue of the fine cooperation of Dr. Sakel and those who are given the opportunity to investigate the problem.

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*Joint Meeting, March 2, 1937*

THOMAS K. DAVIS, M.D., *President of the New York Neurological Society,  
in the Chair*

THE ORGANIC SYNDROME IN THE PSYCHOSES. DR. SAMUEL W. HAMILTON, White Plains, N. Y. (by invitation).

The "organic syndrome" is encountered at every turn. Observers in the neurologic field are studying disturbances in the mental state, to the advantage of diagnosis. Such a disturbance appears incidentally in the course of other disorders—for instance, bromide intoxication or involutional melancholia. Many infectious processes may lead to appearance of the organic syndrome; so may cachexia, valvular disease of the heart, sclerosis of the cerebral vessels and acute

or chronic nephritis. The entire list of exogenous toxins, starting with alcohol and ending with the newest hypnotic, may produce mental symptoms. Probably most arteriosclerotic conditions belong in the large group of organic syndromes, as do the atrophy of senility, the disorganization due to dementia paralytica and lesions resulting from falls and blows.

Mental symptoms may be due directly not to the primary damage but to circulating substances that impair the function of nerve cells at a distance from the primary lesion. Liebermeister's description of fever delirium is sound today. There are headache, oversensitiveness to noise and lights and a feeling of irritation and compulsory relaxation, with which there is slight restlessness. Thoughts seem to flow faster than one wishes, or at least without the control that one usually is able to exert. Then, there may be too much talkativeness and a cheerful attitude. Other patients are troubled when they have difficulty in recollections that ought to come easily. Perhaps it is the recollection of a word only, or perhaps the patient wishes to give an order and cannot quite do it. Then comes the stage at which the patient, on closing his eyes, begins to see unusual things, or perhaps to hear them. When he opens his eyes, he is again clear. Dreams are vivid, and the dreamer is likely to awake in fright. Perhaps he is afraid to fall asleep. Then come illusions—the wall-paper, the ceiling, the carpet or the dress of somebody nearby all seem to contain forms that are not really there. The delirious patient finds it difficult to hold a grasp of the environment. He also has what Bonhoeffer called weakness in the train of thought. Accordingly, he does not put things together correctly and shows difficulties in attention and retention; hence, many sense stimuli are not perceived at all, and others are not properly combined; accordingly, the concept formed may be faulty. In these acute and recoverable states the attention of the patient may be jolted into activity. Indeed, one sees something similar at times in an advanced senile condition or in arteriosclerosis, when the patient, under the influence of a powerful stimulus, may seem much more normal for a time, grasping what is said and formulating his thoughts in intelligible phrases.

Then come more hallucinations—particularly visual, but all fields may be represented. They refer to the usual trends of thought. Some seem to represent changes within the eye itself. The patient appears to visualize a whole scene. No one has told how one can anticipate whether the patient's hallucinatory experiences will be agreeable or terrifying. Soon, the mood fluctuates, so that the sick man may laugh or weep. His restlessness may reach a stage of chorea. At this stage he is likely to feel that he is not ill. If he becomes more ill, his consciousness becomes still more clouded. His motor system is still more irritable, and he may show jactitations. If the illness reaches the last stage, speech becomes stammering and aphasic; movements are uncertain and spastic, and stupor and, finally, coma develop. Sometimes the delirious patient performs a variety of abnormal acts.

A few conditions are typical of the particular toxic agent. The alcoholic patient, for instance, has hallucinations that can be influenced by suggestions of the physician. Many are especially interested in funerals and talk much of having been to, or of expecting to go to, one. Indeed, in delirium there may be elaborate delusional systems, more commonly in alcoholic disturbances. Well known symptoms occur in heart disease with failing compensation. Fear, disorientation, passing delusional formations and sometimes a determined eagerness to get away are noted. Even the cardiac patient may at times be euphoric, though anxiety is the more frequent concomitant of a lesion in the circulatory apparatus.

In many instances mental symptoms precede all others. This has been mentioned in epidemic encephalitis, as in the case of a carpenter who woke in the middle of the night saying: "Do you know who I am? I am God!" (Kasinin). Recent studies have shown that in cases of tumor of the brain the first symptoms may be mental.

A young man presented symptoms leading to a diagnosis of delirium of unknown origin, though several good observers thought that dementia praecox

was developing. Several months later the tonsils and appendix were removed, and soon the patient recovered. Such a history raises several questions: If one makes the diagnosis of an organic syndrome in a young person, he must, of course, seek unremittingly for the locus of possible infection. Ought one, then, to operate on every part of the body that may conceivably be pathologic?

It should be remembered that delirium is more likely to develop in an unstable than in a stable person; that is, the young and the psychopathic are more liable than the old and the stable.

CONSTITUTIONAL ASPECTS OF PARANOID REACTIONS. DR. NOLAN D. C. LEWIS  
(by invitation).

My subject represents a portion of an anatomopathologic investigation of the so-called major psychoses which my colleagues and I carried out in an attempt to discover fundamental or associated tissue characteristics in the various reaction types and, if possible, to establish a more definite differential pathologic picture. The methods of procedure, with the results of the investigation, will be detailed in a series of forthcoming monographs, each dealing with a particular reaction type and attempting to correlate the pathologic tissue changes with the behavioral or symptomatic expressions of the disorder. In these studies the individual person with his many parts is considered statistically; but we have included those most important differences in personality usually neglected in this type of work.

The psychopathologic aspects of paranoia have been described from several points of view by such able investigators as Mercier, Wernicke, Bianchi, Magnan, Krafft-Ebing, Kraepelin, Bleuler, White and Jelliffe, Meyer and Freud. The theories of Freud are of importance in any attempt to understand the psychologic mechanisms underlying the symptoms.

Regarding any possible somatic pathologic change in these states comparatively little has been said, and the isolated observations have been limited practically to certain developmental and chronic conditions of various areas of the brain, none of which has proved characteristic in a study of the group. In postmortem studies of true paranoia, or what might be called the higher forms of the disease, there exists the opportunity to deal with only a few cases, in which the material is rarely available for the investigation of the condition in its early stages, since the patients live out their life span unless accidental death occurs and deteriorate late in life. The deterioration is not even presenile in the average patient. Because of the fair preservation of intellectual contacts, patients frequently are discharged from the hospital, never to return. Therefore, at best, when an opportunity comes for autopsy, there is the possibility that phenomena once prominent are partly or wholly obscured by senile changes. However, in the group of conditions studied, comprising paranoid developments designated in the diagnostic groups as essential paranoia, the paranoid state, alcoholic paranoia and paranoid dementia praecox, there were types of tissue organization, changes and end-results characteristic of the group which distinguish it from ordinary senile and arteriosclerotic conditions, on the one hand, and from the catatonic-hebephrenic dementia praecox group, on the other.

The 188 patients utilized in this study were selected solely on the basis of the mental symptoms and not on that of any diagnostic labeling or final evaluation. I was well acquainted with practically all the patients during life and had first hand knowledge of their life histories and behavior. As the constellations of symptoms fall fairly readily into what is termed paranoid development, it was thought unnecessary to coin new terms for the groups. Moreover, the conditions could be subgrouped into essential paranoia, the paranoid condition, alcoholic paranoia, senile paranoia and paranoid dementia praecox. However, the symptomatic criteria were as rigidly maintained in determining the subgrouping as is possible in any form of personality study, in which one deals with many individual variations.

First, in order to establish as homogeneous a group as possible, patients showing acute confusional episodes, any type of cyclic trends, catatonic or classic hebephrenic symptoms, a known organic disease of the brain or any type of convulsions were excluded at once, whether or not there were projection and hypercompensatory features.

Observations on the circulatory system were of particular interest. The average weight of the heart was 445 Gm., which is high for a group study of any type of material (in thirty-one cases, or one sixth of the total number, the weight was 300 Gm. or below). The enlargement of the heart was due to muscular hypertrophy, frequently complicated by interstitial replacement, calcification and fatty alteration. Chronic valvular disease in the form of sclerosis, thickening or calcification was a constant feature, thus revealing perhaps the effect of the constant strain of life or of previous infectious disease or both. Lesions of the aorta and its main branches were frequently encountered in this group; in fact, in my experience they were sufficiently numerous to justify the conclusion that they are a characteristic pathologic expression of the paranoid group, since in no other mental disorder are so many vascular lesions noted. They included thickening, thrombosis, ulceration, calcification and rupture. Aortic aneurysm was observed in 25 instances (about 14 per cent), which is high for patients supposedly free from syphilis. There was also a remarkable tendency to hemorrhage, thrombosis, varicosities, etc. Lesions of this type may be a part of the paranoid syndrome, resulting from compensation and hypercompensation during the years of mental and physical tension characteristic of the compensatory features of the psychosis.

In two thirds of the cases the brain weighed 1,400 Gm. or over. In many instances the heavy brain showed senile atrophy and arteriosclerotic changes; thus originally, in the earlier years of the patient it must have been still heavier. This may be significant in terms of the total integration. Advanced cerebral arteriosclerosis was present in approximately one half (ninety) of the cases, among which there were ten instances of basilar aneurysm and thirty-six of massive cerebral hemorrhage. In other cases various areas of encephalomalacia resulted from thromboses.

*Comment and Conclusions.*—There are so many aspects of the living person that one may find something in the living form to fit into a frame of any shape, type or dimension. Many investigators interpret these fractional aspects in terms of causes of biologic and pathologic phenomena. I do not desire to leave this impression in regard to the tissue changes I have summarized. Lesions observed in the viscera of the psychotic person may be coincidental and evidence of various diseases; they may be due to the trophic rôle played by the brain in the nutrition of different organs; they may be evidence of some as yet obscure influence exerted by the emotions on structure; they may be the direct result of the mental disorder, as in the ingestion of infective material, filth and other objects, and they possibly may be the local expression of a deeper state on which both the mental disorder and the somatic changes rest. In any analysis of material, there must be kept in mind not only these changes but the question of inherited components, individuality manifested in differential growth of the organism, the organizing ability of special growth centers and the various reactions to environmental circumstances. If in a group of persons carefully selected according to a fairly rigid clinical standard one finds that 60 per cent (112) die of hypercompensatory vascular accidents and disorders, 19 per cent (thirty-five) of carcinomatosis and the rest, 21 per cent (thirty-nine), of other disorders, and if, in addition, one finds that the essential pathologic change in each case consists of hypertrophic, hyperplastic types of lesions, as compared with regressive atrophic, hypoplastic varieties, and that these are associated with a life behavior that can be expressed in corresponding categories, I consider the leads worth following in an attempt to determine the nature of this association. The complete material in any one case would serve as an illustration of the general principle.

**EVALUATION OF THE BIOCHEMICAL APPROACH TO THE PSYCHOSES. DR. WILLIAM H. DUNN (by invitation).**

A survey of the literature on the biochemical findings in the psychoses is reported. Consideration is given to the contributory causes of the confusion that exists in this field. A group of papers selected from the literature on sugar metabolism and oxygen consumption is surveyed, in order to point out the newer trends in research and the clarification that is resulting. In addition, an evaluation is attempted of the nonpsychologic therapeutic methods in use in the psychoses.

**DISCUSSION ON PAPERS BY DRs. HAMILTON, LEWIS AND DUNN**

DR. KARL M. BOWMAN (by invitation): It is not easy to discuss the three papers from any particular approach; I must discuss each by itself.

Dr. Hamilton presented the problem of the organic syndrome and said that not much had been added to the study of this subject in recent years. Most neurologists would agree that Meyer's work is a classic article on the subject to which comparatively little has been added. There should be mentioned a second article, which has attracted little attention in this country but which is valuable. In 1901 Henry Head, in the Goulstonian Lectures, reported on the mental changes which accompany certain types of visceral disease. He described the symptomatology in detail and concluded that in his cases most hallucinations, delusions and changes in the mental state, particularly sudden spells of depression and attitudes of suspicion, arose on the basis of reflex visceral pain.

Another point with regard to the organic syndrome in psychoses is obvious and has been emphasized many times: There is not merely a toxic process but a toxic process associated with a particular type of personality; therefore one will find that in organic conditions the mental symptoms vary according to the personality of the patient. This is shown by the simple illustration of a common infection, pneumonia. One patient with a temperature of 105 F. is clear mentally; another is delirious. The content of the delirium in an organic psychosis will depend on the submerged material of the patient's mind; that is, what will be brought up in delirium will depend on what is there, and therefore the content will vary in individual cases.

Alcohol is another classic example. It will produce elation in one person, irritability in a second, depression in a third and almost no reaction in a fourth. Why do persons respond so differently? When one attempts to think of these different reactions as purely the result of a drug, one sees that the so-called toxic syndrome is not merely an organic condition but that it is determined by personality as well.

The second paper I find difficult to discuss. First, I am not a neuropathologist. Second, such an amount of material was covered in a brief time that the speaker had to omit many details and give mainly conclusions. The correlation which he made between the regressive type of psychoses and regressive pathologic changes and between the compensatory type of psychoses and the compensatory type of pathologic changes is interesting.

In the third paper it was pointed out that in many studies on the relationship of emotional to biochemical changes necessary details have not been considered and little attention has been paid to the exact emotional condition of the patient at the time the study was made. In 1921 I reported a series of studies on the blood chemistry in different psychoses and recorded in detail the emotional state of the patient at the time the blood was taken for study. When I submitted the article to the ARCHIVES OF NEUROLOGY AND PSYCHIATRY, it was returned with the statement that all the material bearing on the emotional state at the time the blood was taken had better be eliminated, for it added nothing to the value of the paper. Perhaps in some of the other papers which Dr. Dunn mentioned in which these details were not given the material was omitted for the reason that editors saw fit to delete it. I persisted, and another medical journal printed the paper with the details.

Dr. Dunn mentioned the study which Dr. Kasanin and I made in 1929 on blood sugar in emotional states (The Sugar Content of the Blood in Emotional

States, *ARCH. NEUROL. & PSYCHIAT.* **21**:342 [Feb.] 1929) and the fact that the findings did not fit commonly accepted ideas, at that time based mainly on the work of Cannon, who stated that in extreme emotional states, such as fear and anger, there is a rise in the amount of sugar in the blood. Cannon (Bodily Changes in Pain, Hunger, Fear and Rage, New York, D. Appleton & Company, 1920) advanced his theory of the increase in the sugar content of the blood in emotional states without making a single estimation of the blood sugar; the theory was based entirely on the fact that he found sugar in the urine of the animals; he assumed there must have been a corresponding increase in the sugar content of the blood, which resulted in the spilling over of sugar into the urine. A number of points could be raised concerning this theory. First, may the renal threshold vary in emotional states? If one assumes that the normal renal threshold of sugar is from 170 to 180 mg. per hundred cubic centimeters of blood, is it possible that it is affected in emotional states, so that in a person who is excited, angry or afraid sugar may spill over into the urine without the level in the blood reaching that of 170 or 180 mg.? There is, for example, the work of a Japanese investigator to the effect that an increase of thyroid extract in the blood affects the renal threshold.

Then there are the questions of the psychotic as compared with the normal person and the nature of the emotional change in the psychoses. In our article Kasanin and I raised the question: May it be that the emotion of the psychotic subject is qualitatively different from the so-called normal emotion; not only psychologically but physiologically? Granted that in normal fear, normal anger and normally extreme emotion there may be a change in the sugar content of the blood, is it possible that the mood of the psychotic person is abnormal and not simply an exaggeration of the mood of the normal person and that, therefore, the absence of changes in the sugar level of the blood is due to the fact that one is dealing with a different condition psychologically and physiologically?

With regard to the question of decreased consumption of oxygen in schizophrenia, Dr. Grabfield and I have several points of considerable interest. Much of the work was done on the basis of accepted standards for basal metabolism, without using specific controls. When we endeavored to use as controls nurses and doctors in the hospital, we found among these subjects so many with low basal metabolic rates that it made us skeptical of some of the previous work. Again, there are various ways of interpreting this. It may be that the average doctor or nurse has not the usual fear of the formidable machinery for determination of the basal metabolic rate and that therefore relaxation is more complete. Hence, the basal metabolic rate is lower.

With regard to the effect of different substances, such as carbon dioxide, sodium amyta and sodium bicarbonate, d'Elseaux and Solomon (Use of Carbon Dioxide Mixtures in Stupors Occurring in Psychoses, *ARCH. NEUROL. & PSYCHIAT.* **29**:213 [Feb.] 1933) reported on work done at the Boston Psychopathic Hospital. I followed that work closely; in the patient who was used for a number of tests it was interesting to note the variation of reactions when different persons were in the room. It was commented on a number of times that with certain persons present the patient did not show the same degree of remission in the specific treatments that she showed when they were absent. It was concluded that there was an important psychologic element in the tests. The carbon dioxide raised the problem of the death threat. The person who is deprived of oxygen, who struggles for breath until thrown into a convulsion, may well be stimulated by the death threat. The mobilization of all the forces of the personality in response to the death threat may be the cause of the temporary improvement, rather than the increased consumption of oxygen. With regard to the reaction of all the patients, it may be interesting to report a case. Because of difficulty in securing a patient with a catatonic condition of long standing, Dr. d'Elseaux studied a man in another hospital who had been in catatonic stupor for several years. He thought the condition would be suitable for carbon dioxide therapy, for if the patient responded well to carbon dioxide the value of the treatment would be proved. He sat down and started to talk to the patient. In a short

time the patient was talking and remarked that this was the first person who had shown him any attention since he had been in the hospital. It was therefore impossible to use this patient to determine the effect of carbon dioxide. I mention the case to show some of the difficulties and sources of error that are likely to occur in work of this kind.

With regard to benzedrine, my associates and I used this drug at the Boston Psychopathic Hospital in certain cases of catatonic stupor. The results, so far as we could determine, showed nothing of value. We seemed to drive the patients from catatonic stupor into catatonic excitement, and if one must make a choice, I think the catatonic stupor is preferable, from the nursing standpoint at least. As far as the schizophrenic process is concerned, I believe benzedrine has little effect. With regard to certain psychoneurotic states and simple retarded depressions, the experience which I have had at the Boston Psychopathic Hospital and that of certain members of the staff at the Bellevue Hospital indicate that benzedrine is of definite value.

DR. WENDELL S. MUNCIE, Baltimore (by invitation): What I shall say is from the standpoint of one whose responsibilities are concerned essentially with the care of patients; the research I have done has been exclusively in that connection.

In regard to Dr. Hamilton's paper concerning the organic syndrome: I think that he and I are on common ground. I divide this syndrome into the reactions caused by poor support of the brain as the integrative organ of the body and the reactions caused by direct and structural damage to the brain. In effect, one has two entirely different types of reaction. In the first type are what Bonhoeffer has described as the *exogene Reaktion*, and in the second, the defect disorders. As Dr. Hamilton's paper concerns essentially the first group, the disorders caused by defect in support, I shall confine my remarks essentially to that group. First, "support" disorders assume a tremendous importance in clinical medicine of all types, and in our branch particularly, because they cover what is underneath, as snow covers everything on the ground. Second, some types of "support" disorders appeal to every one's good sense as being preeminent examples of that group. These are the delirious and hallucinatory types. There are other types in which the variation from this standard is so great that it becomes a matter of clinical definition as to what is the importance, if any, of the toxic factors, if they can be demonstrated. The questions, then, are: When and to what extent are the toxic factors important, and when do they cease to become so? That is a matter which I should like to urge Dr. Dunn's colleagues to tackle, because there is need of biochemical and other laboratory help in this problem. As the problem stands today, it becomes exclusively a question of clinical judgment as to when toxic factors are the important elements in the total situation and when other factors, such as those of personality, are more important. The question of the "support" disorders brings up the scientific controversy between Bonhoeffer and Kraepelin, in which Kraepelin's doctrine demanded a specific psychosis for each specific toxic agent. Bonhoeffer's teachings, on the other hand, stressed the essential likeness of all "support" disorders; modern clinical thinking still shows the division into the two groups. Dr. Harold Wolf and Dr. Desmond Curran, at the Bellevue Clinic, stressed the rubber stamp type of behavior which is seen in all types of "support" disorders. On the other hand, clinical experience, even that of Dr. Curran and Dr. Wolf, I believe, will stress the points which are differentially important, although they are not totally reliable, so that the controversy will still go on. As regards the outcome of "support" disorders Dr. Hamilton stresses the generally good outcome. Ordinarily, it is a kill or cure affair, but it seems to me that three possibilities are present as far as the outcome is concerned: First, the patient may recover completely, when all the factors which militated against his health clear up, and, second, the damage—the toxic effect—may be of such severity or of such long-continued application or have been directed to such parts of the organism as to cause irreparable structural damage and give rise to the defect syndrome. The third possibility has to do with

various types of what one might call "rut" formations—essentially personality disorders, of paranoid, hallucinatory and other types—as chronic sequelae, when clinical intelligence would deny the further importance of toxic factors.

In regard to Dr. Lewis' paper: I am, with Dr. Bowman, impressed and rather overwhelmed by the amount of work that has been condensed into such a short presentation. It is work with which I am not familiar and to which one of my teachers, Prof. Johannes Lange, makes little reference in his excellent work on the problem of paranoia. In recalling the examinations of some patients with conditions belonging possibly to the general paranoid group of which Dr. Lewis has spoken, I must say that nothing remarkable came to light. Nevertheless, in none of the cases was autopsy performed, so I do not have the final statement. Professor Lange mentioned the remarks of a colleague, whose name I do not now recall, to the effect that gross evidences of sexual disturbances are common in patients suffering from paranoia and paranoid states.

I may have misunderstood Dr. Lewis' opening remarks; if so, I beg his pardon; if not, I should like to register this exception to his paper. In case these findings should become universal, which they may well do, I still should register a protest concerning the use of the term "symptomatic" in regard to the patients' clinical behavior as opposed to that of the "more basic" factors in the production of the changes observed at autopsy. I do this because my philosophy of human behavior does not allow behavior as such to be put in the class of epiphenomena. Dr. Lewis, I think, agrees with me, and I probably misunderstood him.

With regard to Dr. Dunn's paper: My connection with the biochemical studies has been strictly that of one interested in the clinical phase. My feeling about it from this standpoint is that diagnostic tests, such as the dextrose tolerance curve, are helpful when they work. This may sound foolish, but an illustration will show what I mean. When one has a patient in the hospital for several weeks in whom repeated dextrose tolerance tests give practically normal curves and the patient one afternoon attempts suicide, much to every one's surprise, and when one looks back over the record and finds that the day before the dextrose tolerance curve was unusual, though nobody paid much attention to it, such evidence counts. The trouble is that other persons who try suicide may not have the same sort of curve. My belief is that emotional reactions express themselves in various ways. In some persons it is in the dextrose tolerance curve; in some, in the unstriped musculature of the eyelid, and in some, in totally different ways, so that one needs a variety of tests which will take account of practically every method of observation; then one will merely watch each individual patient to see in which way he reacts.

In regard to the therapeutic use of the various drugs which have been mentioned: I have had experience with some; there, again, I take perhaps the middle road—they are all right when they work, and sometimes they do. Personally, I have never made light of the attitude of the person who dispenses such drugs. I had an enlightening example recently, when I took over the care of a young woman who had previously been under the care of a colleague. We are of different temperaments, and the previous treatment had revolved around a philosophic resignation to a rather bad situation and had worked for a while. The patient finally came to me again, and under the stimulus of current interest at the clinic, I gave her benzedrine; she became so elated that she was afraid to use the drug any longer and discontinued it. She has tried benzedrine several times since, at my request, with opposite effects. It is to be noted that I did not go to her; she came to me, asking for treatment. I gave her this therapy, with immediately good results, which did not persist when I came to know her better; I have finally been forced to the same ground that my predecessor took, namely, that she must make the best of a difficult situation. That is about where I stand on the present use of various therapeutic agents.

DR. SAMUEL W. HAMILTON: When one discusses organic phases of psychoses, one shows that there is uncleanness as to where the organic field stops. Much has been said tonight about dementia praecox: For instance, what is the oxygen

content of the fluids of the body in this disease? This is a field in which there are many doubts. I agree with Dr. Muncie's kindly phrased statements about the organic syndrome, and I wish particularly to say that what he points out about the differences in the individual patient might well have been more stressed. He has properly emphasized that. Of course, one finds all sorts of combinations of symptoms, and the difference in these combinations lies exactly where he placed it.

DR. NOLAN D. C. LEWIS: It was of necessity that I left out a great many important data. I could have spent the evening, for instance, on the changes and individual variations in one gland. I remember that four or five years ago I described a case of epilepsy before the American Psychiatric Association; at that time it was, I think, the only case which had been worked over from all known angles. There had been years of investigation of the family history and the clinical symptoms, and the patient was given a thorough psychoanalysis, an exhaustive chemical study of the body fluids, physical examinations and roentgenograms without number. Finally, complete autopsy with microscopic study of the body systems was made. I sorted the material and presented it in a comparatively short paper showing the method I have used for years in performing autopsies in these cases, but I did not want to publish it, unless I could report the complete case, to demonstrate that one should study the individual patient with all available methods. Any one who would like to try this method of study should cooperate with the clinician, and the clinician should record his findings in the same terms that the pathologist uses in balancing his impressions of the tissue reactions—in terms of regression and of hypercompensation—as applied to the whole person, or in any other way that gives a picture of how these reactions balance. The examiner will not be able at autopsy to tell the types of delusion and hallucination and what kind of home situation the patient had. I believe, however, that the individual person has a characteristic integration, that there are constellations which extend all the way through and that one may find the universal in every particular or in every fundamental. As to the terminology, I agree with Dr. Muncie. I have to use terms that I do not like. They infer differences which one does not want to emphasize and differences which are not really valid, in our way of thinking. They are too static; they are not fluid enough, yet one does not like to coin new terms. I agree that the total organism must be taken into consideration, but I am convinced from my work that there is still evidence of the total pattern in the structures of dead tissues. I do not think that postmortem pathology is complete at present.

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#### PHILADELPHIA NEUROLOGICAL SOCIETY

*Regular Meeting, Dec. 18, 1936*

FREDERIC H. LEAVITT, M.D., *President, in the Chair*

PAINFUL HEMIPLEGIA: A CONSIDERATION OF CENTRAL PAIN. DR. ALFRED GORDON.

The observation submitted here presents another of the many examples of difficulty in diagnosis when one is confronted with a destructive cerebral lesion. It also leads to the conclusion that each case must be judged on its merits and that the localization of pain and dysesthesias is a problem that cannot yet be solved with facility.

*History.*—M. C., a middle-aged man, fifteen years ago had an apoplectic seizure with loss of consciousness, which lasted four days. There was right hemiplegia with aphasia. Since, he has gradually recovered speech and power in the affected extremities, although not fully. Two or three years ago there developed pain in the upper extremity on the affected side, which has been continuous, with periods of exacerbation.

*Present Status.*—The patient is hemiplegic; use of the leg is much better than that of the arm. The right hand is deviated to the ulnar side and presents concavity of the palm. Active extension of the fingers is possible, but they do not remain in that position; when the patient makes an effort to extend them, muscular contraction increases, and they do not extend fully. When the hand is outstretched, slight choreic and myoclonic movements with tremor are observed. Power in the hand is limited (the patient is right handed). He is able to perform many movements with the upper right limb, although after ataxic attempts. The biceps reflex is obtained with difficulty. The triceps reflex is normal. Hoffmann's reflex is absent. The right knee jerk is increased. There is no ankle clonus; the plantar reflex on the right is variable, appearing at times in flexion and at others in extension. The right abdominal reflexes are abolished.

There is an atrophic state of the entire right upper extremity and of the adjacent musculature of the thorax and shoulder. The right hand is continuously cyanosed.

Examination for subjective and objective sensibilities reveals: The patient complains of absolute intolerance of his hand to cold and, to a much less extent, to heat. A cold object placed in the hand gives him excruciating pain, and on cool days the exposed right hand gives considerable discomfort. There is also lack of tolerance to cold objects, such as ice, when applied to the arm and forearm, but to a less extent than when applied to the hand. Moreover, the least weight placed in the right hand or on the forearm is intolerable, while the left hand does not react in this manner. Pressure on the individual fingers of the right hand provokes pain. The stereognostic sense of this hand is only slightly impaired. There is some ataxia in the right hand, as seen in the finger to nose test. Test with a compass reveals slight errors in the right hand. Objective sensibility is not seriously involved, as compared with that of the left hand. Objective sensibility in the right lower extremity is normal. The cranial nerves are intact. All biologic tests of the blood and urine gave normal results. The eyegrounds show angiosclerotic changes.

*Comment.*—The character of pain which the patient experiences reminds one of causalgia. Since Déjerine, and especially since Roussy, Head and Holmes, algias and perversions of sensation have been observed chiefly in cases of involvement of the thalamus, particularly in the external nucleus, according to Déjerine, and in the inner nucleus, according to Head. According to these observers, the centers for gross and elementary sensibilities are the basal ganglia, while the cortex possesses a function of higher order, namely, fine discrimination of various sensibilities. However, there is accumulated anatomicoclinical evidence which favors the opinion that the preceding contention is not absolute, that types of dysesthesia corresponding to identical localizations do not exist and that there are cases of so-called thalamic disturbance in which, from the standpoint of sensitivity, the cortical syndrome is present and cases of cortical involvement in which the thalamic syndrome is present. From the clinical angle, careful perusal of a large number of cases of verified thalamic disturbance shows that there are: a pure hemianalgesic form with no other sensory disturbances; a form of hemianesthesia with gross vasomotor manifestations and involuntary movements—myoclonic or choreo-athetotic—with or without signs of pyramidal involvement; a form with deviation of the hand, and a form with symptoms of striate disturbance. Marie also described a cerebellothalamic form.

In following the course of development of this group of symptoms in the present case, I venture the opinion that the initial trouble was a hemorrhagic attack in the left internal capsule, which gave rise to unconsciousness and terminated in hemiplegia and aphasia. The extent of the lesion was slight, as can be seen from the considerable regression of contracture and the paralysis with absence of the extensor plantar reflex. Gradually, softening of the tissue extended to the median line and involved the thalamus, which several years later produced a syndrome typical of that described by the original observers under the name "thalamic syndrome."

The case is interesting from the standpoint of the presence of all the classic symptoms of Déjerine's syndrome. It is instructive from the fact that such a group of symptoms may develop several years after an initial apoplectic insult, with regressive paralytic manifestations. Finally, spontaneous pain in a limb which is suffering from an old central lesion is of a special kind; it suggests the central extension of a long-standing lesion, usually to the nuclei of the thalamus. As to the physiopathogenesis and modus operandi of the dysesthesia: The accompanying vasomotor manifestations suggest incrimination of the sympathetic nervous system. This system possesses special sensibility. In the patient under discussion the objective hemihypesthesia is evidently due to the original involvement of the sensory fibers during the capsular apoplectic origin. The coexistence of vasomotor disturbances corroborates the contention of sympathetic involvement. In the light of present knowledge the thalamic area constitutes a part of the center of the sympathetic nervous system.

#### DISCUSSION

DR. TEMPLE FAY: It is difficult to discuss this problem, as I have not examined the patient. True thalamic pain is unique. Dr. Gordon has described a type of hemiplegia which Fulton attributed to injury of the large pyramidal cells near the rolandic fissure. This produces a flaccid, rather than a spastic, type of hemiplegia, the latter being produced by injuries to the premotor area or to the descending pyramidal pathways. This strongly suggests that the disturbance in this case involved the cortex rather than the deeper regions of the brain. A tingling and burning projection pain can be obtained from stimulation of the ascending parietal convolution. In many instances the true type of thalamic pain differs in that contacts to the skin produce dysesthesia of a painful nature.

DR. ALFRED GORDON: I wish to ask Dr. Fay if, in severing sensory and motor nerves, he has observed pain which he attributes to the sympathetic nervous system.

DR. TEMPLE FAY: I hold a definite view regarding what is known as sympathetic pain. I believe that pain fibers pass through the sympathetic system to join eventually the usual pathways in the cord, but their ganglion cells are not in the sympathetic chain, even though the fibers find this system a convenient pathway to their termination along the blood vessels and deep structures in the body.

Most fibers for this type of pain find entry into the spinal cord between the first and the fifth thoracic segment; hence, they may traverse the vascular tree or sympathetic pathways for some distance to reach a point of entry but are not otherwise segmental or closely identified with the sympathetic pattern. My interpretation of causalgia is, first, that it is a burning, tingling type of pain, which, if it follows peripheral nerve patterns, is usually concerned with irritation of the posterior roots. However, a similar type of pain is noted with vascular disease and involvement of the pain fibers on the blood vessels.

This is the type of pain encountered in so-called "amputation neuroma," which persists after destruction of the peripheral nerve to the part; rhizotomy renders all superficial tissue objectively anesthetic, but the patient continues to complain of excessive tenderness to deep pressure and a burning type of pain.

I have found that chordotomy below the fifth dorsal segment does not obliterate the pain, even in cases in which rhizotomy and section of the peripheral nerve have been accomplished. If, however, chordotomy and section of the anterolateral column on the opposite side are performed above the first thoracic segment, complete relief from the pain can be obtained. This has been verified by controlled ascending spinal anesthesia.

Pain persists in this area, even though anesthesia is raised to the nipple line. Above this point, pain begins to diminish in the stump of the lower extremity, and when anesthesia has reached the ulnar area on the hand, or the eighth cervical segment, pain is completely relieved. In fact, clinical relief is greatest in the lower

extremities when anesthesia in the axilla, or the third thoracic segment, has been obtained. This, I believe, explains the confusion that has existed and modifies Foerster's concept of collateral pain pathways in the cord.

In my opinion the pain fibers follow the large blood vessels into the abdomen and thorax, leaving the vessels to enter the spinal cord between the first and the fifth thoracic segment. This may explain variable results obtained by ganglionectomy, in that destruction of the sympathetic chain helps to interrupt the fibers as they pass by the cord at this level.

I believe the rational means of relief is that of chordotomy above the first thoracic segment.

DR. ALFRED GORDON: I wish to call attention to the observations of Foerster, Altenburger and Kroll that after unilateral sympathectomy lowering of sensory chronaxia was noticed on the same side. Claude Bernard, Dusser de Barenne and Tournay showed that pain is observed in areas in which sensitivity has been abolished by sectioning sensory nerves. Of course, Dr. Fay's opinion is authoritative; nevertheless, even the best authorities sometimes disagree. As for causes of causalgia: Leriche experimented with cutting sections of the outer membranes of arteries containing sympathetic fibers, with relief from pain. These are a few facts to contradict some of the opinions expressed.

#### INJECTION OF ALCOHOL INTO THE GASSERIAN GANGLION. DR. G. M. DORRANCE.

In 1916 I reported the technic of injection of alcohol into the gasserian ganglion for the relief of tic douloureux; I have been using this method since. For the past fourteen years I have used it also for the relief of pain in the distribution of the fifth nerve, especially pain caused by malignant disease or its treatment. I can say that as one gains experience with the improved instruments now available, the number of successful injections increases. My record of successful injections is over 90 per cent in the past five years.

I think that in equally experienced hands this method is as safe and satisfactory as division of the sensory root and that in cases in which the risk is exceedingly poor it should take the place of that operation. I find it possible many times to make injection into the lower part of the ganglion so as not to involve the first division, but I prefer injection into the sensory root as a rule. I draw attention to the fact that at the time of injection one is never sure that there will not be retraction of the area of anesthesia on the next day. By this I mean that one believes he has made injection into the first, second and third divisions, only to discover on the next day that there is only partial loss of sensation in the first division, while the second and third divisions retain complete anesthesia. However, if dilatation of the pupil of the eye occurs at the time of the injection, one may be confident that injection has reached the sensory root. I have occasionally seen temporary paralysis of the sixth nerve for a few minutes, without understanding the cause. I have not seen paralysis of the seventh or the third nerve. I have had ocular complications, but these were in no part due to the injection itself; rather, they were secondary to the insensibility of the eye to foreign substances. I always advise the patient to wear a shield over the eye to guard against such complications.

At present I have almost given up injections into the outside branches. Once in a while I make injection into the inferior dental nerve for some special reason or into the mandibular branch outside the skull, but I do not attempt injection into the second branch, and I do not like to make injection into the third branch outside the foramen.

I do not know any one who can regularly make an injection into the second division. I think that one only spills alcohol around the branches of the second division of this nerve and that relief lasts only a comparatively short time, whereas if one injects alcohol into the nerve the duration will be from fifteen to eighteen months. Furthermore, it is difficult to make injection into the ganglion after the outside branch has been treated.

My method follows the general idea of Hartl, except that I use a heavy trocar needle. Using Hartl's guide on the pupil of the eye and the condyle of

the jaw, I introduce the needle 2 cm. from the angle of the mouth and 1 cm. above this point; with the finger inside the mouth I guide the needle back until it touches the base of the sphenoid bone. I then draw the tip of the needle over the body of the sphenoid bone until it comes to the pterygoid process. The tip is then gradually drawn backward off the pterygoid process into the foramen ovale. It is difficult to describe this technic. One can gain it only by actual practice on the cadaver.

When the needle enters the foramen, there is a peculiar sensation, as though it were passing through soft cartilage. Once one experiences this sensation one will never mistake it. As soon as the needle enters this cartilage, I stop. To inject the alcohol, a long needle is substituted for the trocar. If one wants to affect only the lower part of the ganglion, it is necessary to make injection very slowly. Here will be noted first loss of sensation in the third division. If one injects more alcohol at this time, one obtains complete anesthesia of all three branches. If this is not successful, one gradually introduces the needle a little farther, injecting as one proceeds until anesthesia has been produced in all three branches. Many persons seem to think they can introduce a needle similar to a spinal puncture needle directly into the foramen. After many years of work on cadavers and injections in patients, I devised a heavy trocar needle with which I can practically always enter the foramen ovale.

The pain produced by introduction of the needle makes injection difficult for both the operator and the patient. I adopted the use of first stage chloroform anesthesia to overcome this and have found it satisfactory. Before starting the operation one should instruct the patient to raise his left hand every time one touches him with the point of the needle, so that when the area is tested for sensation after the injection, he will respond properly.

I first reported 11 cases in 1924 and can now report 34 cases in which injection was satisfactorily performed. I know I have made a great many more injections into the ganglion, but my records are not complete. Fourteen injections have been made this year. I present reports of 8 of them tonight. Some were partial, but in most instances injection was made into the sensory root.

In my opinion, if one injects alcohol into the sensory root, it has the same effect as dividing this root. The anesthesia is permanent. It is my impression that I have made more than 100 injections into the ganglion in different clinics. I have records of 4 cases in which I was unable to introduce the needle into the foramen ovale. I believe that injection into a sensory root is permanent and that injection into the ganglion will last for several years and is likely to last permanently.

The conclusions I draw are from my experience, since I am unable to give complete records. I believe that injection should be made into the ganglion in preference to any of the outside branches; one should attempt to reach the lower part of the ganglion, if one wants only the third division. I have had no deaths and no complications except the conjunctivitis and keratitis secondary to a foreign substance entering the eye without the patient's consciousness of its presence.

#### DISCUSSION

DR. TEMPLE FAY: I believe that this is an important method of injection in certain instances. I have seen patients to whom Dr. Dorrance gave injections who enjoyed the same type of relief that is obtained by surgical section of the posterior root. I wish to ask several questions.

Dr. Dorrance spoke of making injection into the root. If the needle passes through the ganglion so as to engage the root fibers, what assurance is there that the alcohol will not only paralyze the motor and sensory roots but pass into the region of the base of the brain and involve other cranial nerves? The root of the trigeminal nerve floats freely in spinal fluid contained within the sheath and bathes the posterior aspect of the ganglion. Alcohol in this area would, therefore, in my opinion not be confined to the ganglion or its root.

Second, how often does herpes occur after such an injection, and is there additional danger of herpes to the eye? The Patrick method of peripheral injection into the third division is usually successful; the Byrnes method of injection into the second division I have found to be accurate and to result in few failures. In cases of malignant disease Dr. Dorrance's method is desirable.

I have, however, given up injection into the peripheral branches of the nerve for the relief of major trigeminal neuralgia because it is of only temporary value and subjects the patient to excruciating pain.

The Frazier operation is simple and permanent, and the mortality is less than 1 per cent.

I shall be glad to refer patients who prefer injection to operation to Dr. Dorrance for relief by the method of injection into the ganglion.

DR. WILLIAM DUANE: My experience with Dr. Frazier taught me a great deal about injection. He taught how to avoid anesthesia of the first division by partial section of the posterior root; I, personally, would far rather have injection of alcohol in the manner in which Dr. Frazier did it—with the first division left free and injection into either the second or the third division. I have on several occasions made a good injection into the third division, and the alcohol has seeped back to the ganglion, producing anesthesia of the first division for a day or two. Operation has no terrors for me if injection of alcohol fails.

DR. R. A. GROFF: I subscribe to what Dr. Duane has stated. I think that by far the best method is injection into the second and third divisions peripherally. The old method of gasserian ganglionectomy used before Dr. Frazier and Dr. Spiller devised section of the root resulted in the serious complication of keratitis, with loss of the eye. As I see it, in connection with injection into the ganglion, not only is this complication to be feared, but others, such as blindness, palsy of the third and seventh nerves and sometimes paralysis of the auditory or vestibular nerves, may occur. The objection to injection into the ganglion is therefore more serious than simple excision of the ganglion and should give way to injection into individual peripheral nerves.

DR. F. H. LEWY: I wish to ask Dr. Dorrance whether he has observed cases of so-called paresthesia.

DR. B. J. ALPERS: I wish to ask what is the longest period of relief—should one speak of it as permanent?

DR. F. C. GRANT: I congratulate Dr. Dorrance on very skilful work. I believe particularly in what he has done for the relief of pain from malignant disease about the face and mouth; under these circumstances the merciful thing for the patient is to block the trigeminal nerve. Afterward, it is amazing how such patients can eat—free from pain—the treatment they will tolerate and the way in which they will put on weight. They can sleep and eat without disturbance, and it makes a tremendous difference. I have not had much experience with injection into the ganglion. The reason that I have not used it with frequency is that it is harder to do; even in Dr. Dorrance's hands the alcohol may dribble back along the root and involve other nerves. Cushing reported a number of cases in which all the cranial nerves on the side of injection were involved. I have seen facial paralysis follow injection into the ganglion; so I believe that it is a real danger—however, one must also admit that in the operative procedure facial paralysis is not an unknown complication. The question is which is the better. When a patient has a carcinoma of the face and the operator is as skilful as Dr. Dorrance, it seems to me that injection into the ganglion is the ideal procedure. How long do the patients lose sensation? I know of a case in which Dr. Frazier made injection into the ganglion in 1924, and the patient has been free from pain since. He writes me because of paresthesia in the face; it is very cold where he lives, and he worries lest his face will freeze. Reports in the literature of cases in which anesthesia lasted twenty years are not unknown. Results from injection into the ganglion—putting aside the potentialities of danger—seem to run closely parallel with those obtained by

operation. For single trigeminal neuralgia I prefer operation. In cases of cancer of the face one can often make injection into the peripheral nerve and give relief, and the relief may last long enough, for either the patient may recover from the pain phase or the cancer may kill him in the length of time the relief lasts. Certainly, in such cases something must be done, and injection of alcohol in the hands of an experienced man like Dr. Dorrance is as satisfactory as operation.

DR. G. M. DORRANCE: I became interested in the treatment of tic douloureux by injection because so many patients objected to the more formidable operation. Aside from this indication, injection is extremely valuable in painful conditions, such as carcinoma in the distribution of the fifth nerve in older patients who are too weakened to submit to division of the sensory root. I frequently see herpes, but it is never sufficiently intensive to be termed a complication. I also observe headache following injection, but not so severe that it does not respond to ordinary medication.

I have known patients to experience "crawling" sensations in the face, but never the burning of severe paresthesia. Temporary paralysis of the sixth nerve is an interesting phenomenon. Since it lasts only a few minutes, it does not appear to be caused by direct chemical effect of the injection. I think that it is due rather to pressure.

SUBARACHNOID HEMORRHAGE WITH SPECIAL REFERENCE TO PAPILLEDEMA: AN EXPERIMENTAL AND CLINICAL STUDY. DR. JOHN Q. GRIFFITH JR. (by invitation) and DR. W. E. FRY (by invitation).

Papilledema did not occur in any of 11 cases of subarachnoid hemorrhage studied, although the elevation of spinal fluid pressure and the duration of observation appeared adequate. In 78, or 66 per cent, of 118 cases reported in the literature papilledema did not develop. In this series the findings in 16 cases, or 14 per cent, were equivocal, while in 24 cases, or 20 per cent, definite papilledema appeared. Of these 24 cases the diagnosis was confirmed at autopsy in 7, in 3 of which there was known to have been hypertension. In 2 other cases glioma of the brain was observed, and in 1 case a large unruptured aneurysm was thought to have acted as a tumor.

In previous work we showed that kaolin injected intracisternally into rats prevented (1) the passage of thorium dioxide, injected intracisternally, along the perineural spaces of the optic nerves and (2) the appearance of papilledema in the presence of growing cerebellar tumor. After experimental subarachnoid hemorrhage, thorium dioxide was blocked from entering the perineural spaces of the optic nerves in 15 of 20 rats. It was inferred, therefore, that blood in the spinal fluid, if present in sufficient amounts, tends to block the perineural spaces of the optic nerve and prevent the development of papilledema. In a minority of cases, however, the block is incomplete, and papilledema may occur if other predisposing factors are present. Among these we suggest: (1) partial ventricular block, so that relatively little blood reaches the subarachnoid space; (2) malignant hypertension; (3) glioma, and (4) sinus thrombosis. Illustrative cases are cited.

DISCUSSION

DR. TEMPLE FAY: Dr. Griffith and Dr. Fry are to be congratulated on presenting evidence regarding papilledema that requires considerable thought and analysis. Behr in 1915 presented a theory based on the effects of obstruction along the vaginal sheath of the optic nerve or the effects of increased intracranial pressure on transmission of lymph fluid along the nerve. Swift in 1930 pointed out the importance of venous stasis arising in the cavernous and sigmoid sinuses. This is a problem on which ophthalmologists have not yet agreed, and the type of experimental animal gives variable results.

I believe that Dr. Walter Lillie favors the Behr theory. It seems to me that Dr. Griffith and Dr. Fry have shown in this instance that when the vaginal

sheath is protected by occlusion, the incidence of papilledema is less. Perhaps because of physical obstruction, fluid along the sheath has been blocked from intracranial transmission. However, a state of papilledema may be expected to arise secondary to venous thrombosis.

I wish to ask the authors how they explain the subsidence of choked disk with the beginning of atrophy of the optic nerve, even though intracranial pressure persists and the vaginal sheath can be shown to be distended. Papilledema occurs from conditions other than intracranial pressure, and increased intracranial pressure does not always produce papilledema. I wish to have their views on this paradox in the problem.

DR. W. E. FRY: In answer to Dr. Fay's question and discussion: The report of the literature and the theories in regard to papilledema published by Holmes a few years ago summarized well the work done previous to them. They emphasized the presence of two factors: pressure on the vessels as they cross the vaginal sheath of the optic nerve and pressure within the sheath transferred to the sheath from the increased intracranial pressure. In choked disk occurring with thrombosis of the central vein of the retina, the picture is different. As a rule, there is elevation of the disks, but it does not look like the choking seen in association with intracranial trauma. Frequently, one sees cases in which there appears to be papilledema without increased intracranial pressure. I think that in some of these cases the condition is not papilledema but neuritis of the disk. In regard to subsidence of papilledema after atrophy: I think there is an overgrowth of glial tissue which contracts and flattens.

DR. J. Q. GRIFFITH: In respect to Dr. Grant's remarks: Perhaps the important point is the duration of block. In my experiments the longest period between the first subarachnoid hemorrhage and injection of thorium dioxide was fourteen days. It is possible that the papilledema occurring in trauma may come after the original block has subsided. Dr. Fry has answered Dr. Fay's questions better than I can.

#### ATROPHY OF THE PARIETAL AND CEREBELLAR LOBES ASSOCIATED IN CERTAIN CASES WITH MULTIPLE SCLEROSIS. DR. MICHAEL SCOTT.

In the 900 encephalographic studies that have been made by the neurosurgical staff at the Temple University Hospital, many interesting cortical patterns have appeared. Certain characteristic changes in the cerebral and cerebellar conformations have been noted in several clinical states and have been confirmed by operation in many instances.

Attention has been called by Dr. Temple Fay to an unusual pattern arising in certain cases of multiple sclerosis, and I shall present a series of clinical cases of multiple sclerosis that illustrate this phenomenon. In the encephalographic pattern in this condition there has appeared repeatedly a defect in the parietal area associated with loss of cortical substance, as well as definite diminution in the size and contour of the cerebellum. This has been termed atrophy in view of the appearance, which suggests loss of volume of brain substance.

In addition to the preceding combination of areas of involvement, encephalographic films show enlargement of the ventricles and many points of atrophy throughout the frontoparietal areas of the brain. However, this additional pattern is encountered frequently in posttraumatic, syphilitic and chronic inflammatory states.

That the encephalographic findings are in accord with the cerebral and cerebellar changes observed at autopsy by others in cases of multiple sclerosis may be seen in the following excerpt: (Brain, W. Russell: Critical Review: Disseminated Sclerosis, *Quart J. Med.* **23**:343 [April] 1930):

"The cerebral cortex may be involved by patches of subcortical origin, or by surface patches, wedge or arch-shaped, which coalesce to yield a moth-eaten

appearance. In these cortical areas demyelination often corresponds to areas of supply of the superficial vessel plexus of the cortex. Similar changes are found in the cerebellar cortex."

Brain also stated that Merle and Pastine and Siemerling and Raecke described dilatation of the ventricles as frequent. Conaway and Hill reported observations at autopsy in 11 cases of multiple sclerosis. They described cortical atrophy in the frontal and parietal lobes, as well as in the cerebellum. In these areas and in other parts of the brain and cord they saw scattered plaques, from a few millimeters to 2 cm. in diameter, some of which showed degeneration, with softenings and cavitation. Dilatation of the ventricles was also frequent in their cases.

The distinctive encephalographic feature in cases of well established multiple sclerosis appears, therefore, to concern the combinational relationship between the parietal lobe and the cerebellum. Atrophy of the parietal lobe alone is relatively frequent in many conditions other than multiple sclerosis. Cerebellar atrophy or shrinkage is likewise fairly frequent in the child as well as in the adult, but the combination of the two, associated with a slotlike defect in the parietal area, usually bilateral, is, in my opinion, a finding which should suggest strongly the possibility of multiple sclerosis, when clinical confirmatory signs are present in neurologic manifestations, the eyegrounds, vision and the colloidal gold reaction. When the clinical signs are equivocal, the encephalogram has been a means of ruling out other types of cerebral pathologic change, as well as tumor and chronic disease of the spinal cord.

During encephalography a Queckenstedt test and the injection of air determine that no block exists in the spinal canal. If complete drainage is obtained, the entire spinal cord can be visualized with the roentgen technic devised by Dr. Edward Chamberlain. In cases of multiple sclerosis in which operation has been performed the cord itself appears at times to be unusually small. The silhouette of the spinal cord in studies made with injection of air has helped to confirm this fact.

Protocols, as well as Dr. Chamberlain's description of the encephalograms, are presented in 6 cases which, it is believed, are instances of multiple sclerosis.

#### DISCUSSION

**DR. EDWARD CHAMBERLAIN:** When Dr. Scott first gave me his ideas in regard to encephalography in these cases, I was antagonistic to the suggestion that the roentgenologist could help the neurologist in cases of multiple sclerosis with encephalographic studies. It seemed to me that much work must be done before correlation could be proved and that there would probably be found a good many other conditions giving a similar appearance. Dr. Scott has gone back to the gross pathologic picture, and this should be used as the basis for learning to read roentgenograms. When Dr. Scott showed me what he found, I became interested. A great deal of work remains to be done before one has anything diagnostic. However, at present, after I have gone through the laborious process of studying the degree of correlation between such findings as these and the diagnosis of multiple sclerosis, I can say little except that I have had another demonstration that one must learn to read. One cannot overdo the matter of reading gross pathologic changes. So far, there has been difficulty in obtaining comparisons between postmortem observations and encephalographic findings. For one reason, a slight change in the size of the brain can make much difference in the subarachnoid space. When I talk about diffuse cortical atrophy, of which one speaks so glibly, I sometimes say that there are veritable holes in the brain tissue, but one cannot make correlation with postmortem observations. Either the roentgenologist is wrong or the pathologist must study these brains in a different way. I think there is such a thing as diffuse cortical atrophy. If the brain is just a little shrunken when taken out, as compared with the cavity, there is discrepancy in size; on the other hand, diffuse cortical atrophy is difficult to demonstrate at autopsy. It is the same in any type of shrinkage

of the brain. If one administers to the patient a hypertonic salt solution one obtains the same picture. It would be interesting for some one to count brain cells and see if any are missing.

DR. M. A. BURNS: I do not feel enthusiastic about this presentation. I was surprised to hear Dr. Scott speak of the marked cerebellar atrophy; yet in only 1 of his cases did he speak of the presence of marked staggering gait. If one is to accept the presentation of marked cerebellar atrophy according to the encephalograms, one should expect to find definite cerebellar ataxia. Dr. Scott spoke of an ataxic-spastic gait in 5 cases—much like that one would observe in a typical case of multiple sclerosis—but in all 6 cases he described marked cerebellar atrophy. I cannot connect the pathologic process of such marked degree with so few physical signs, especially in the gait.

DR. A. GORDON: The diagnosis of multiple sclerosis is made in some of these cases before encephalograms are carried out. I wonder whether the symptoms Dr. Scott described in some cases cannot be accounted for by the changes in the parietal and frontal lobes and the cerebellum. Why should one maintain the diagnosis of multiple sclerosis? No autopsies were performed. Moreover, histories of the condition of the patients, prior to coming to the hospital, are not given. I believe one could explain all the symptoms from the roentgen pictures without recourse to the diagnosis of multiple sclerosis.

DR. SAMUEL HADDEN: I am glad that Dr. Chamberlain and Dr. Burns sounded notes of caution in the interpretation of these encephalographic findings, for I do not believe that one should consider them as specific in multiple sclerosis. Many diseases may present the same changes. I shall show films in 2 cases which I described before the society in 1931. The pictures show an extreme degree of parietal and cerebellar atrophy. There is also a slight degree of atrophy in the frontal lobes, but the parietal and cerebellar atrophy is so extreme that I am sure there would be gross evidence of atrophy in these regions at autopsy. As in Dr. Scott's cases, there was marked excess of cerebrospinal fluid in both these cases. The patients, who were brothers, showed a picture typical of Marie's cerebellar ataxia, and there was a family history of definite involvement. At the approximate time the encephalograms were taken, similar studies were made in cases in which my associates and I believed multiple sclerosis was present. As a result of these studies we expressed the belief that encephalography offers a means of differentiating between multiple sclerosis and cerebellar ataxia. I am sure we were just as wrong at that time as Dr. Scott is at present in placing too much emphasis on the encephalographic findings. More necropsies must be performed and larger numbers of cases studied before proper evaluation can be made.

DR. B. J. ALPERS: I think this contribution by Dr. Scott represents a type of curiosity that is worth while. There are certain questions, however, which I wish to ask regarding the clinical findings.

First, in the cases which he described the condition could easily be diagnosed as multiple sclerosis without recourse to an encephalogram, but I presume that he has reported the most characteristic examples, in order to make his point clear. From the clinical standpoint the question arises: In what types of cases of multiple sclerosis could the encephalographic picture be of value? I must confess that I can see nothing in these encephalograms to indicate any characteristic findings.

In respect to the question of cortical atrophy in the encephalogram, I think one is on dangerous ground. I wish to congratulate Dr. Chamberlain on his attitude with regard to the significance of atrophy as seen in encephalography, for I believe that one must be cautious in interpreting it.

Last year I presented encephalograms in a case of marked atrophy of both frontal lobes in which there was shown at autopsy almost no atrophy but a marked pad of fluid in the subarachnoid space in both frontal areas. I am convinced that in these cases one should speak of "encephalographic atrophy,"

in order to make it clear that its significance is not known, if, indeed, it exists at all in most instances. What appears to be atrophy in an encephalogram is really not atrophy at all. I should question the significance of the findings in these cases and even whether atrophy would be seen if one were to hold the brain in his hands. It is unusual to see cortical atrophy in cases of multiple sclerosis unless there are complicating factors, such as cerebral multiple sclerosis; so I am skeptical of these findings.

DR. HELENA E. RIGGS: Because my associates and I have had difficulty in correlating encephalographic and postmortem observations, I have studied the brain in relation to the skull whenever possible. There is correlation between the so-called convolutional atrophy seen in encephalograms and observations made post mortem.

It is not possible to evaluate encephalographic findings with the gross changes in the brain unless the specimen is seen *in situ*. The best gross evidence of atrophy of the brain is dilatation of the subarachnoid space, which disappears as soon as the space is opened in removing the brain from the skull. Grossly, convolutional atrophy is apparent only in advanced stages, since a compensatory overgrowth of astrocytes occurs. Microscopically, I have observed close correlation between the encephalographic findings and loss of functioning ganglion cells in the cortex. When a differential diagnosis must be made between increased intracranial pressure due to tumor and that resulting from circulatory insufficiency, the encephalogram, or even the roentgenogram of the skull, is of more value than the clinical findings. Edema of the brain due to neoplasm is relatively rapid, while that resulting from cerebral circulatory stasis is extremely slow. When there is marked molding of the skull, especially in the middle fossae and around the clinoid processes and dorsum sellae, with osteoporosis along the venous channels, a vascular basis for clinical symptoms must be considered.

DR. TEMPLE FAY: Irrespective of the encephalographic pattern, Dr. Scott has called attention to the fact that in certain cases of advanced multiple sclerosis similarity of defect appears in definite areas. As to the interpretation of the films from the standpoint of atrophy: Dr. Scott has pointed out that the amount of spinal fluid drained in all but 1 case was greatly in excess of the normal.

The average normal encephalogram yields from 105 to 125 cc. of spinal fluid, when complete drainage is obtained. In all but one of these cases as much as 200 cc. or more was obtained, and one is faced with the fact that the extra space occupied by this fluid must represent either shrinkage of the brain tissue or atrophy.

Certainly, the skull does not grow away from the brain, leaving the brain behind and allowing an excess of fluid to fill the space. If these brain patterns are normal, one must account for the excess of fluid, or if the excess of fluid represents a loss of substance, the term "atrophy" may be used justly, in the same sense that one finds loss of tissue volume in an arm or a leg after it has been incased in a tight plaster cast.

It is the function of the neuropathologist to diagnose the pathologic changes which have occurred. Grossly, the films indicate atrophy, and this atrophy occurs in rather characteristic areas. The patients in this series were selected from a group that were considered, clinically, to have multiple sclerosis; the diagnosis was made in accordance with Dr. Spiller's principle that all other conditions must be carefully ruled out.

I am of the opinion that the stereoscopic films indicate an unusual amount of tissue loss and atrophy in the parietal and cerebellar areas in a combinational relation, whereas in other patterns the defects are widespread and do not involve these particular areas to the same degree.

DR. F. C. GRANT: There is much free comment about pathologic observations based on encephalographic films, but, in the last analysis, no one has made

1,000 normal encephalograms. Until this is done, one has no business to talk of fine details or abnormalities. The work is interesting as far as it goes, but it needs confirmation.

DR. M. SCOTT: There is one thought I wish to leave. I had no intention of giving the impression that we make a diagnosis of multiple sclerosis by encephalography alone. All realize that complete studies in these cases are necessary. I wished to point out that the encephalograms show interesting changes; whether or not they are diagnostic of multiple sclerosis only future studies will prove. I had wished to present these observations as reports of cases, but, through a misunderstanding with the secretary, they were scheduled as a paper. As to Dr. Burns' question regarding signs of cerebellar disturbance: The conditions in this presentation were diagnosed as multiple sclerosis by competent neurologists. Many of the patients showed signs of cerebellar involvement. In the complete charts I think that one can go back and pick up many symptoms and signs that I did not give here because of lack of time.

Dr. Hadden brought up the question of cerebellar ataxia. In none of the cases presented here tonight was any hereditary or familial history of multiple sclerosis shown.

I am glad that Dr. Grant pointed out that the findings are of interest but that more cases are needed; that is exactly my opinion.

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#### CHICAGO NEUROLOGICAL SOCIETY

*Regular Meeting, Jan. 21, 1937*

FRANCIS J. GERTY, M.D., *President, in the Chair*

THE PROBLEM OF NEURITIS. DR. F. H. LEWY, Philadelphia (by invitation).

This presentation, which is based on clinical observations and neurologic and chemical examinations, started with the observation that despite the clinical variety of peripheral nerve diseases, their histopathologic features are uniform. Primary inflammatory processes of the peripheral nerves are unknown. Therefore the term neuritis is erroneous and should be replaced by neuropathy. With refined methods of examination, such as graduated hairs and thorns and chronaximetry, neuropathies can be demonstrated in many exogenous and endogenous intoxications and infectious diseases. Their appearance is accompanied by the increase of ketones and pyruvic acid in the blood and urine. Both these products point to a disturbance in the intermediary carbohydrate metabolism. The increased output of ketones indicates the gradual depletion of glycogen in the liver, and the increase in pyruvic acid seems to be a direct consequence of the absence of vitamin B. The pathogenic mechanism of the neuropathy, therefore, seems to be as follows: First, various primary etiologic agents—*infectious, toxic and metabolic*—act on the liver. The liver cell becomes depleted of its glycogen and, simultaneously, of its vitamin B content. Then the stage is set for a neuropathy. Second, avitaminosis B appears as the only form of neuropathy. However, the neuropathy is not the only sign of avitaminosis B. In addition, there are: (1) the so-called general symptoms, (2) physical signs and (3) evidence of systematic degeneration in the spinal cord and basal ganglia. The same phenomena have been found and discussed in connection with the following groups of diseases: (1) disturbances of metabolism, e. g., in diabetes, alcoholism, pregnancy, cachexia and hunger; (2) pernicious anemia; (3) poisoning with heavy metals, such as lead, manganese, arsenic and mercury; (4) infectious diseases, e. g., yellow fever, typhus, typhoid and paratyphoid, streptomycosis and diphtheria, and (5) some constitutional hereditary forms of neuropathy.

From hunger experiments and clinical evidence, I deduced a constitutional and individual glycogen lability and stability, which may be responsible for the varying resistance of the nervous system to infections and intoxications.

#### DISCUSSION

DR. G. B. HASSIN: Should the term neuritis be abolished in favor of such a name as neuropathy? There is a tendency in the East to substitute such names as encephalopathy and neuropathy for certain pathologic conditions in the brain and spinal cord. While it is true that in the majority of types of polyneuritis the degenerative element predominates, the presence of degeneration does not exclude an inflammatory process; that is, degeneration and inflammation are often combined. As there is still a controversy, especially among the Germans, as to what is to be called inflammation, it would be better to retain the old convenient name neuritis.

Have the histologic changes in the spinal cord and the peripheral nerves mentioned by Dr. Lewy been described by the most recent investigators? That is, have his observations been substantiated by reliable pathologic studies?

DR. MABEL G. MASTEN, Madison, Wis.: If one accepts the theory of avitaminosis as the common factor in all neuropathies, how is one to explain the anatomic localizations peculiar to each form of peripheral neuritis (or neuropathy)?

DR. F. H. LEWY: Experimental work shows that feeding rats with liver of normal, well nourished animals prevents hypovitaminosis B, while feeding liver of starved, intoxicated or chronically infected animals does not.

With reference to Dr. Hassin's question, I may say that a number of papers of earlier and of recent years, such as those from Yale, have reported histologic studies. I am in favor of renewed histologic examination of the spinal cord in cases of avitaminosis B with better methods, although the changes are massive enough to be demonstrated satisfactorily with the older technic. It has been my aim to present a number of facts from a definite point of view. However, I consider this synopsis not as final but as a first step in uniting divergent problems under one heading. It is my hope that it will stimulate further studies to confirm, correct or refute these ideas.

As to the nomenclature—neuritis or neuropathy—I agree that this is not an important point to those who know all about it. But, in my opinion, it is different when one considers the teaching aspect. Words have magic power. Dropping the ending "itis" from diphtheria proved helpful in directing attention from the infectious to the toxin-antitoxin complex of this disease.

Dr. Masten's question touches a point of special interest. I do not think that my assumption that all neuropathies are caused by a vitamin B deficiency, through the medium of a liver defect, should exclude the possibility of a specific affinity of various toxins for one nerve or another, thus producing a place of minor resistance. Another phase of the problem worth considering is that most of the vitamins are bound to organic substances and must be activated by heavy metals in order to become effective within the body.

DR. ROY R. GRINKER: Professor Lewy's endeavor to bring these conditions—buried under the "waste-basket" term of neuritis—into a nosologic entity of common etiology is commendable. However, he has gone to the other extreme and included under avitaminosis conditions not similar in nature. There are many false premises in his argumentative attempt to link all the parenchymatous degenerations of the peripheral nerves into one group. Perhaps I am most interested in the relationship of combined cord degenerations accompanying primary anemias and the neuropathologic changes associated with pellagra. There is considerable disagreement concerning the rôle of vitamin B deficiency in the production of changes in the cord (Zimmerman, Mellanby, Grinker and Kandel). However, in none of the experimental work was there observed the pathologic picture typical of human subacute combined cord degeneration (described by Davidson). Certainly, human pellagra, a recognized vitamin B deficiency, never produces the changes in the cord seen in pernicious anemia.

Other discrepancies in the material presented here lead me to disagree with Dr. Lewy when he tries to show that neuritis does not exist, even though one recognizes the importance of vitamin deficiency in the production of peripheral nerve syndromes.

DR. CLARENCE A. NEYMAN: How does Dr. Lewy explain the fact, now well known, that fever promptly brings about a cessation of most choreiform manifestations? A temperature of 105 F. induced during two eight hour sessions cures most mild forms of chorea. This has been shown in over 75 cases reported in the literature.

DR. F. H. LEWY: The question of treating chorea is not directly related to my topic. I agree that I saw good results with fever therapy, but I also saw failures.

If Dr. Grinker failed to produce lesions in the spinal cord of rats, this is in accordance with the experience that the rat during avitaminosis B apparently behaves differently in many ways from other animals. It is also in keeping with the fact that the lesions produced by the Japanese authors were limited to a comparatively small number of monkeys, thus showing that not all factors in this deficiency are known as yet. These include: first, the degree of hypovitaminosis B; second, its duration, and, third, the participation of the various compounds of the B complex. I did not state that avitaminosis B is the cause of all the diseases cited. I said that one should consider to what degree avitaminosis B plays a part in these diseases. It was my intention to give the trend of my thought in the neuritis problem and to show the directions in which, in my opinion, research is promising.

**MARIE'S ATAXIA (OLIVOPONTOCEREBELLAR ATROPHY): CLINICAL AND PATHOLOGIC CONSIDERATIONS. DR. G. B. HASSIN.**

This paper was published in full in the June 1937 issue of the ARCHIVES, page 137.

**THE EFFECTS OF SODIUM AMYTAL AND OTHER DRUGS ON THE REACTIVITY OF THE HYPOTHALAMUS OF THE CAT. DR. JULES MASSERMAN (by invitation).**

This paper was published in the March 1937 issue of the ARCHIVES, page 617.

**DISCUSSION**

DR. GEORGE W. HALL: I know nothing about the experimental work which has been carried out by Dr. Masserman, but he has used the term "amytal" and "sodium amytal" without discriminating between the two preparations. The sodium amytal, as is the case with ipral calcium, is much more prompt in its action than the amytal or ipral.

DR. PAUL C. BUCY: Dr. Masserman has presented a beautiful confirmation of the fact that the hypothalamus is intimately concerned with the manifestations of emotional disturbance. In the past, the work of Ranson and others on the hypothalamus has dealt with it as a whole, with no attempt to determine the particular functions of the different parts of the hypothalamus. It is an extremely intricate structure; that it functions as a unit is inconceivable. I wonder whether Dr. Masserman is able to give any information as to what nuclei are concerned with the different effects which he has obtained? The observation that sodium amytal is selective in its effect on the excitability of the hypothalamus, while leaving the excitability of the pyramidal tract relatively unaffected, is of interest because of a similar differential effect on the precentral cortex. There one finds that the barbiturates suppress the excitability of the extrapyramidal tracts, while leaving the pyramidal tract relatively unaffected. This has been explained as due to the action of the barbiturates on the subcortical centers on which these cortical extrapyramidal tracts terminate. Dr. Masserman's work, demonstrating a selective depressant effect of sodium amytal on the subcortical centers in the hypothalamus, lends support to that hypothesis.

DR. ROY R. GRINKER: When I first initiated the program of research of which this work forms a small part, it was not for the purpose of confirming the experiments of Ranson, which were beautifully complete in themselves. In visiting and studying at several European and American clinics, I was struck by the fact that hypothalamic function, when clearly elucidated, will furnish the beginning of a union between neurophysiology and dynamic psychiatry. Others before me have already expressed this naively hopeful concept. I was particularly struck by Foerster's stimulation of the human hypothalamus at operation, resulting in changes in cortical activity. Furthermore, sodium amytal, when slowly injected intravenously, aroused stuporous catatonic patients for a few moments; as a member of the barbiturate group, it presumably had its effect in the hypothalamus. However, lately Martha Vogt and others have expressed doubt of the selectivity of the hypothalamus for barbiturate action. I, therefore, wished to determine whether the excitatory effect of amytal was located in the hypothalamus or the cerebral cortex itself. However, marked changes in threshold value were not found in either location, so that these experiments do not serve to solve the problem for which they were devised. I seriously question whether they add much to the problem of localization within the hypothalamus.

DR. JULES MASSERMAN: The only drug used in my experiments was sodium amytal. Amytal is insoluble and was not used.

With regard to the localizability of the reactions to specific tracts or nuclear groups in the hypothalamus, I think that the experiments do not speak one way or the other, since the reactions observed were probably massed. This was indicated in later experiments by the fact that, when the tissue immediately about the point of the needle electrode was destroyed by electrocoagulation, the reactions of the remaining hypothalamic tissue to injection or to the spread of the faradic stimulation were altered but not abolished.

Dr. Grinker's comments need no further discussion.

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*Regular meeting, Feb. 18, 1937*

FRANCIS J. GERTY, M.D., *President, in the Chair*

SUBCORTICAL PREFRONTAL LOBOTOMY IN THE TREATMENT OF CERTAIN PSYCHOSES.

DR. WALTER FREEMAN and DR. JAMES W. WATTS, Washington, D. C. (by invitation).

Prefrontal lobotomy, as devised by Egas Moniz in 1935, has been performed by us in 20 patients, who have now been observed for more than two months. Physiologic alterations following the operation have been notable especially in the peripheral circulation. Cold, moist, cyanotic hands tend to become pink immediately after the operation and to remain so for a considerable period. As one patient expressed it: "I used to pile on the covers till I'd nearly suffocate, but I couldn't get my feet warm. Now they're warm all the time." In one case auricular fibrillation due to rheumatic heart disease disappeared, and a presystolic murmur became audible for the first time. Marked alterations in blood pressure have also been observed, e.g., a fall in systolic pressure from 170 to 140 mm. Favorable changes have also been observed in distressing gastro-intestinal symptoms, such as indigestion, bloating, constipation and hemorrhoids.

Of the psychologic effects, abstract thinking, constructive imagination and synthetic ability seem to be impaired to a greater degree than more fundamental thought processes. Patients can name colors rapidly, add columns of figures correctly, remember recent and remote events exceptionally well and concentrate on tasks with less effort than before. Response to problem stories show correct recall of details but defect in synthesis. Agitation is reduced in all cases. Patients in panic and catatonic states have become much more accessible. In one

case the operation on the two frontal lobes was performed at an interval of one week. There was no relief from the catatonic picture after operation on the right side. After the second operation, performed without anesthesia, a change occurred instantly, although the patient remained catatonic for two days. Thereafter, she improved progressively—accepting food on one day, eating it by herself on the next, washing herself on the next day, walking on the day after, talking on the tenth day and using the telephone on the fourteenth day. She has now resumed life in the family circle.

Obsessions and compulsive behavior have shown immediate improvement, although in some cases there have been relapses. The old phobias have returned progressively in some instances, and episodes of excitement, particularly in schizophrenia, make adaptation to working impossible at present. Whether improvement will occur later in these cases is questionable. Five of 6 patients are not improved. One died after the operation, of cerebral hemorrhage, and another is in a hospital for mental disease because of an attempt at suicide.

Of the 20 patients operated on in 1936, 7 are substantially well after from two to five months; 5 are improved; 7 are not improved, and 1 is dead. One patient has monoplegia involving the hand. Affective disorders offer a much better prospect than schizophrenia. The outstanding result is reduction in the obsessive nature of the painful ideas. Signs of intellectual deficit are not pronounced and do not handicap the patient for ordinary occupations of routine nature.

#### DISCUSSION

DR. ERIC OLDBERG: As far as my personal credulity is concerned, I should like to see at least 100 patients with various mental aberrations used as a control group; that is, a bur hole would be made through the skull, but the dura would not be opened and no damage would be inflicted on the frontal lobes. The bur hole could be used for subsequent procedures, if indicated. The results in such a series, if negative, would add considerable weight to those obtained in the authors' series of 20 cases of lobotomy.

I wish to ask the authors if they believe that their operation would be just as effective if performed only in the predominant hemisphere rather than bilaterally.

DR. EDMUND JACOBSON: I wish to ask Dr. Freeman whether he or his associates or Dr. Moniz has performed many two stage operations, first taking out the button and then sending the patient home in the belief that he has had a complete operation. This would furnish a test as a control; the patient could return later and go on with the operation. The reason for doing this is the apparently nonspecific character of the operation. Surely, an instrument introduced in the way Dr. Freeman described, first on one side and then on the other, will remove regions of tissue in one operation differing from those in another.

I wish also to ask for more complete information regarding the classification of the cases described.

DR. LOYAL DAVIS: Unfortunately, the only report of the procedure which Dr. Freeman advocates available to me was that in *Time*. I had hoped that the reports were grossly exaggerated and that some physiologic facts would be given as the basis for indications for the operation and for the results which have been obtained.

It is not clear to me just what is attempted in this operation. The only explanation given so far is that of a patient who said that Dr. Freeman removed his "worry center." Have the short association fiber tracts between adjoining gyri been sectioned, or does the lesion involve one of the four large intracortical association fiber pathways? I assume that Dr. Freeman's experience as a pathologist has made him curious to know the exact location and extent of the lesions he produces. As a pathologist, he may not have much fear of looping out pieces of subcortical tissue, but his statement that one patient died after the operation of cerebral hemorrhage and that in many instances blood vessels are pulled out with the wire loop gives one's surgical conscience a slight twinge. The offhand

manner in which this surgical procedure is described and discussed is no credit to the essayist as a surgeon, a pathologist or one who is searching for a scientific truth.

It seems to me that a surgical operation proposed to neurologists and psychiatrists of this country as a method of treating patients with certain psychoses should be presented with the observance of all the strict conditions of a physiologic experiment. As I see it, this has not been done.

DR. ALFRED P. SOLOMON: Because of studies that Dr. Darrow and I have been making with the galvanic skin reflex in psychotic patients, I am interested in Dr. Freeman's report that in some patients there was suppression of the secretion of sweat after the operation. Is it possible that, associated with the surgical procedure, there was trauma, transient or otherwise, to the efferent fibers to the sweat glands?

I am not convinced that the description of the patient's behavior following operation is indicative of a therapeutic result which cannot be explained otherwise.

I suggest that the euphoric gratitude that some patients exhibit after prolonged sleep and insulin shock is comparable with this type of result. I believe that evaluation of the clinical results obtained by Dr. Freeman would involve careful study of each psychosis and predication of the possibility of spontaneous remission or reaction to suggestive therapy. I have observed that certain persons with psychogenically determined psychoses exhibit hypersuggestibility and are susceptible to many types of "cure."

DR. CLARENCE A. NEYMANN: I am impressed with the fact that, according to Dr. Freeman, all patients exhibit after treatment a certain amount of what may best be called dementia. This mental deterioration was evidently not measured accurately. Psychologic tests exist with which it might have been measured, even if the patient had a mild psychosis before treatment. I refer especially to the tests which measure the intelligence of the superior adult.

It also occurs to me that the psychotic types which Dr. Freeman has mentioned do not usually result in dementia. I therefore wonder how much dementia was brought on as the direct result of the operation. It is known that psychoses rarely develop in feeble-minded persons and that psychoses due to organ disease of the brain become less pronounced as dementia progresses. Patients with dementia paralytica who express expansive grandiose ideas lose many of these ideas as the dementia progresses, and they lapse into a purely vegetative existence. I therefore wonder whether the results reported by Dr. Freeman are attributable to actual dementia based on a change in the finer personality traits.

I saw many patients in the World War in whom loss of the frontal lobes, or part of them, resulted in a labile kind of dementia associated with a tendency toward a bizarre kind of merriment and a propensity to play pranks and to pun. Perhaps this change in personality so often associated with injury to the frontal lobe is the reason that Dr. Freeman's patients have gained better control of their emotions.

DR. CHARLES F. READ, Elgin, Ill.: Dr. Freeman emphasized the mental tension relieved in these cases. I wonder what is the effect on blood pressure and whether he would recommend operation in essential hypertension in young subjects.

DR. HARRY A. PASKIND: In my ignorance of matters neurosurgical, I rise to ask why the operation was done on the brain. It has been known for years that many patients with psychiatric disorder improve after trauma, intercurrent disease or surgical operation, only to relapse later. I think that the operation would have been just as successful if done on the hands, or even on the feet.

DR. CHESTER W. DARROW: The suggestion has been made here that the decrease in sweating of the hands following this operation was the consequence of destruction of efferent tracts from the cortex containing excitatory sweat fibers. This would imply that the frontopontocerebellar tracts from the premotor area were injured, since these tracts were found by Langworthy and Richter to mediate

sweat reactions to direct cortical excitation. It may be that Dr. Freeman can say whether it is likely that these tracts would be injured by his procedure. I wonder, however, whether he would consider what seems to me the more likely alternative: that the operation might in these cases free the premotor cortex from the excessive chronic inhibitory action of the more frontal regions, leaving the premotor cortex free to exert its normal inhibitory control over subcortically determined sweating.

DR. LEWIS J. POLLOCK: For many years I have heard of many types of treatment for the psychoses, and I have realized the shortcomings of neurologists and psychiatrists in offering any hope for the amelioration of many types of these psychoses. There is no doubt that any method which may lead to hope of relief should be welcomed; on the other hand, I think that without definite and positive proof of the amelioration of the psychoses it would be immoral to offer to the public any sort of procedure which would awaken expectation and hope without possible fulfilment. On what does this procedure rest? First, this is not an operation but a mutilation. Moniz said he was unable to state the exact extent and location of the parts removed by the leukotome. That is evident, for there are different sizes of skulls and of brains, and there is no way of knowing what may be removed. The wire loop may strike a blood vessel; it may loop about the cannula or do many other things. Unless one sees the lesion produced by the leukotome, there is no means of knowing what is removed. At times, it has been necessary to reoperate on patients to destroy areas left intact at a former operation.

What is the anatomic basis for the procedure? It is known that persons with a lesion of the frontal lobe present psychic symptoms. Therefore, the frontal lobe is the home of the psyche. When frontal lobectomy has been done in cases of tumor, it has been said that no measurable mental defect can be found. If, therefore, one is dealing with a psychosis, mutilation of the frontal lobe can result in no ill and the psychic symptoms will disappear. To me this seems extremely loose reasoning. A patient, a Methodist minister, had been a prominent member of the church and was a man who had had great intellect, with rigid principles. He was brought to me because he had had a change of personality. Formerly, he would never go to a movie or into a home where cards were being played—now, quite the contrary. He likes movies, likes to see people play cards and has none of the feelings he had before. But is he a functioning minister? No, and he never will be, for he has a tumor of the frontal lobe. When that is removed, he may be complacent, but he will never be a functioning minister.

The cases in which the best results are said to be given are those in which anxiety is relieved. It is proposed that here is a sort of fixed physiologic pattern, an obsessive complex giving rise to affective reactions along conditioned pathways. When one physically interrupts these pathways, the anxiety and other symptoms disappear. I see no reason to invoke a supposition of this sort, since spontaneous remissions occur frequently. One of Moniz' patients had experienced two previous attacks of depression, one of which lasted for two years. At the expiration of two years of the recent depression the operation was performed, and the man recovered. Who can say he would not have recovered within six weeks if left alone? Many patients with recurrent depressions are highly competent and contribute largely to science, literature and art. Ought one to remove the frontal lobe to relieve a state of anxiety or depression which may disappear spontaneously? What will be left of the musician or the artist when the frontal lobe is mutilated?

If an operation is indicated for a definite purpose, it should be performed. If it is indicated that some association processes should be severed, this should be done by open operation, the exact parts being visualized and severed, and bleeding should be stopped. One should not work in a haphazard way—not knowing what one is doing, whether the patient will have bleeding into the brain or whether one has reamed a vessel supplying cortical centers. These vessels are to a large extent end-arteries.

I am sorry to feel it necessary to talk so vehemently regarding this procedure, but I would not think it honest of me if I did not.

DR. WALTER FREEMAN: A brain can stand a good deal of manhandling. If this is mutilation, as has been claimed, one is mutilating it less with subcortical leukotomy than with the transection of the frontal lobes that has been proposed. We wish not to argue with those who accuse us of surgical phrenology or of carrying surgical therapy to extremes but only to point out that patients with these psychoses are in a serious condition and do not have much chance of recovery otherwise. I refer particularly to the obsessions and depressions that go on year after year with little change except a gradual increase in the disability. I do not recommend operating on a patient with manic-depressive psychosis, if there is a history of remissions in the past. I do not recommend operating in involutional depression during the first year. Our results in schizophrenia have been unsatisfactory, 5 of 6 patients being unimproved.

Prefrontal lobotomy is not a "shock" operation in the ordinary sense. The temperature may rise to 101 F. after operation. The pulse is not influenced. We have seen little change in blood pressure, but in one instance a pressure of 170 mm. fell to 140 mm. I do not recommend the procedure for essential hypertension, for I do not believe it would work. When an operation like this is compared with operation on the hand, the foot or the abdomen as "shock" treatment, I propose to differ. If the trouble is in the head, why work on the belly?

I called attention to the sweating because in the case used as a control in which a two stage operation was performed, the phenomena were ipsilateral. I do not know what the explanation is. In regard to the controls suggested, the most rigorous would seem to be the drilling of holes on both sides and performing the leukotomy on one side. According to experiments on animals and operative results that have been recorded, it is necessary that both hemispheres be injured for significant results to appear.

As to Dr. Neymann's question regarding dementia: I am not sure I follow him. He may have methods of measuring dementia. Our patients are able to carry out certain tests put to them in a standard way, but in other tests requiring more constructive imagination they fail. These are psychologic tests, and I am unable to report on any but the immediate results. According to the work of Ackerly, the performance improves as recovery occurs.

Is this operation justifiable? We have based our work more on the social than on the psychiatric findings. We have performed operation when the patient faced prolonged or permanent disability and when the type of occupation did not require much constructive imagination. Most patients after operation have been able to adjust better socially than before. I present this as an interim report of our first cases and do not draw conclusions, since it is only with more extensive experience that one can arrive at anything definite.

#### CARBOHYDRATE METABOLISM IN EPILEPSY. DR. LEWIS J. POLLOCK and DR. BENJAMIN BOSHES.

The occurrence of convulsions in states of hypoglycemia, either spontaneous or as a result of the injection of insulin, has focused attention on disturbance of carbohydrate metabolism as a possible factor in producing the epileptic state. The sugar levels during fasting and the response to stimulation with dextrose and insulin were studied in a group of patients suffering from epilepsy. The lack of a technic standard among all workers and the tendency to discuss abnormal findings as "diabetic" or "prediabetic," even though diabetes is not present in the subject tested, make difficult interpretation of our findings in terms of physiologic dysfunction.

*Conclusion.*—In a series of 93 patients suffering from epilepsy the dextrose levels during the fasting were within normal limits. There was no relation between this level and the age, weight or sex of the patient. There was no relation between the dextrose levels during fasting and the precedence or suc-

cession of attacks, nor could the levels be correlated with the type of epilepsy—organic or idiopathic. Oral dextrose tolerance tests were performed on blood obtained from the finger in 91 of these patients. The readings fell essentially in the normal zone. Twenty-six per cent gave high curves; 21 per cent, low curves, and 53 per cent, normal curves. The same lack of correlation noted in the studies on sugar during fasting was observed here. There was no evidence of increased or decreased tolerance. Further work in large groups of normal patients is indicated to determine the significance of the various curves obtained with the dextrose tolerance tests. It is possible that when such studies are made, the variability of our curves may assume importance in relation to possible defective homeostasis of the body to stimulation with dextrose. Glycosuria during the dextrose tolerance test occurred in 20 per cent of the cases. There was none at fasting levels. The renal threshold for our patients averaged 188 mg. of sugar per hundred cubic centimeters of blood. This is slightly above that given for normal subjects. There was no evidence of decreased tolerance.

Insulin tolerance tests performed by the subcutaneous method on 70 patients revealed a tendency to attain the lowest level at the end of the first hour and a distinct failure to return at the end of the third hour. No correlations with age, weight, type of epilepsy or other factors could be found in the response of the patient to insulin. The insulin tolerance test seems to indicate failure of homeostasis because of the relatively many instances in which there was failure of the sugar to return to a fasting level or to return at all for three hours. These curves should be compared with others obtained subsequently in a large series of normal subjects. Hypoglycemic states produced in 70 patients failed to precipitate epileptic seizures. Concentration of bromide in the blood, at high or low levels, failed to produce any alteration in the dextrose levels of the blood.

#### DISCUSSION

DR. VICTOR E. GONDA: I wish to ask why blood from the finger is called arterial blood. How is it possible for the needle to escape the capillaries and veins?

DR. WILLIAM G. LENNOX, Boston: I am glad this study has been undertaken. Twelve years ago I spent a year studying the blood sugar and the sugar curves in epilepsy and arrived at much the same conclusions as have been presented here, but in recent years accusing fingers have been pointed at the sugar levels in epileptic patients. Speaking of mutilating operations: I wish to add to the list the removal of the tail of the pancreas simply because the patient was enough of an individualist to have a low blood sugar curve.

I am sure the authors do not intend to leave the impression that because levels of sugar in the blood and urine are essentially normal, sugar is in no way concerned with the problem of epilepsy. In these experiments they were dealing with body fluids, whereas in epilepsy the fundamental disorder is in the chemical reactions of the functioning neuron. If changes which have to do with carbohydrate metabolism are drastic enough, convulsive seizures occur. No one who has seen schizophrenic patients in the depths of insulin shock pass into all sorts of epileptiform seizures can fail to believe that such a shock can bring out dramatic manifestations. Such reactions, however, do not parallel the sugar levels of the blood. I recommend to the authors and other workers in this field that they examine blood from the internal jugular vein—blood which has recently passed through the brain. The problem is to know what is going on in the functioning neuron, and one approaches nearer to neuronal activity by recording the electrical responses of these cells. It would be a simple matter to determine the effect of the blood sugar level on such electrical activity. Gerard, in animals, found that injection of insulin results in cerebral rhythms which are large and slow and approach the type which Dr. and Mrs. Gibbs and I observed in petit mal seizures. In order to prove that alterations in concentrations of sugar are specific abnormalities which exist in the discharging neurons of epileptic persons, one must know much more about the physicochemical properties of living cells. The electrolytes would seem to be of the most potential significance.

DR. ALFRED P. SOLOMON: I wish to ask the authors whether they believe that the occasional good clinical results obtained with the ketogenic diet in the treatment of epilepsy are in cases in which they have described normal sugar metabolism or whether they believe that the clinical results occur independent of the hypoglycemia induced by the low carbohydrate intake in this diet, solely because of the ketosis.

DR. LEWIS J. POLLOCK: I think that the ketogenic diet works not so much because of the change in the amount of the blood sugar as because of the production of certain acid bodies in ketosis and that the depressive effect of these bodies is at work. What we wished to demonstrate was not the change in carbohydrate metabolism but the need of gathering a large series of cases, from the standpoint not only of comparing diabetic and prediabetic curves with normal curves but of correlating various types of curves, such as the high, and the high delayed, with bodily change in general. Then the curves which we have described may have value.

DR. S. A. SZUREK: That further study of carbohydrate metabolism in human physiologic processes is necessary, as suggested by Dr. Pollock and the variability of sugar tolerance curves reported in this paper, is indicated also by the responses of psychotic patients to insulin therapy. In a limited number of patients being studied to test the new insulin shock treatment, doses ranging up to 190 units have been given without any sign of convulsions. The studies are far from complete, but it has repeatedly been observed that patients do not show signs of coma or convulsions after these large doses of insulin. The question arises whether this is evidence of a striking abnormal condition in these patients or whether similar resistance to hypoglycemia may be found in persons who presumably have no disease.

DR. BENJAMIN BOSHES: Regarding Dr. Gonda's question: It is a matter of experience that curves obtained for blood from the finger are similar to those obtained for arterial blood.

Regarding Dr. Szurek's question: The response will depend a great deal on how much dextrose is available to meet the change in insulin.

The question concerning measurement of the glycogen content of the liver is perhaps answered best by reference to recent work on the relation of the liver to carbohydrate metabolism. It would appear that the dextrose level of the blood is the important factor as regards the response of the liver. If the level is high, the liver is "depressed," and glycogenesis from glycogen is diminished. It is conceivable that the effect of diminution in the level of the blood sugar as a result of the administration of insulin may in some cases cause hyperproduction of dextrose by the liver. Thus, large doses of insulin may not be followed by low dextrose readings, if the blood is drawn after the liver has responded.

#### MENINGO-ENCEPHALITIS. DR. CHARLES F. READ.

The report of another case of encephalitis associated with rubella is added to the limited literature on this subject. Six cases are added to the list of those collected by Merritt and Koskoff in May 1936, bringing the total number in the literature up to 18. Death occurred in 2 instances—11.1 per cent of the cases. Although the percentage of cases in which encephalitis developed is small, the possibility of this complication should be kept in mind, especially in view of the frequency of rubella and the apparently innocuous character of the disease.

Additional references to cases not included in the review of Merritt and Koskoff include: (1) Merritt, H. Houston, and Koskoff, Yale D.: *Am. J. M. Sc.* **191**:690 (May) 1936; (2) Epstein, A., and Loup: *Rev. méd. de la Suisse Rom.* **50**:161 (March 10) 1930; (3) Potter, Olive: *Brit. M. J.* **2**:1084 (Dec. 27) 1930; (4) Gourdon and Guillaume: *Soc. de méd. mil. frang., Bull mens.* **27**:116 (April) 1933; (5) Briggs, John F.: *J. Pediat.* **7**:609 (Nov.) 1935, and (6) Baumgartner, E. A.: *New York State J. Med.* **36**:907 (June) 1936.

## DISCUSSION

DR. ERICH LIEBERT: In one of the cases discussed by Dr. Read, which was reported in the literature by Briggs, who sent two slides, infiltrations were present around the blood vessels, especially the veins. These consisted of lymphocytes, a few plasma cells and some leukocytes. There was no marked glial reaction, as far as could be judged from hematoxylin stains.

DR. G. B. HASSIN: I have had no experience with encephalitis associated with rubella, and should like to know how and by whom the diagnosis of rubella was made. For instance, was any adenopathy present in Dr. Read's patient?

DR. CHARLES F. READ: The diagnosis of rubella was based on the fact that the man had what he described as a eruption resembling rubella at the time of an epidemic of this disease and was able to go to work within a couple of days. He did not consult a physician until the onset of encephalitic symptoms.

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DETROIT SOCIETY OF NEUROLOGY  
AND PSYCHIATRY

*Regular Meeting, Jan. 21, 1937*

MARTIN H. HOFFMANN, M.D., *in the Chair*

RELIGIOUS DELUSIONS: REPORT OF A CASE. DR. H. A. REYE.

*History.*—So far as could be ascertained, there was no history of psychoses or of manic-depressive swings in the antecedents of the patient. She was the only child of wealthy parents. She was a dreamer and lived quite removed from the realities of life. She shared a taste for art with her father and subsequently showed unusual artistic talents. She was always gentle and obedient and, until her marriage, practically went no place without her mother. She was never trained for independence, self-reliance or objective thinking.

She was completely unprepared for marriage. She had always dreamed of it as a beautiful companionship, based on tenderness and understanding. The actual experience of marriage came as a great shock. Its physical aspects frightened and nauseated her. She found the realities of life very different from her dreams. Her sexual inabilities, the children and the household duties all bewildered her. Her husband, who was very virile, was naturally rather dissatisfied with her frigidity and lack of response.

Since he was a Catholic, she became much interested in this faith after her marriage. She hoped that joining the church would bring her closer to him and help her solve the difficulties she encountered in marriage. Though it did not fulfil all her expectations, she found much solace in her religion, which gave her promises of ultimate reward for self-sacrifice, meekness and obedience.

This stood her in good stead when she discovered her husband's unfaithfulness. Her situation later became complicated by the renewal of an old friendship with an artist whom her husband engaged to make portraits of the children. They had much in common and fell in love. Here, however, she came in conflict with her ideology. She fought desperately to tear this guilty love out of her heart. All these conflicts, together with the debilitating effects of an attack of pneumonia, led, in my opinion, to the first confusional exhaustion psychosis, which lasted about six weeks.

She recovered but learned little from this breakdown, for her conflicts and unhappiness persisted. She continued to respond with meekness and humility to her husband's domineering and frequent outbursts of temper. However, she gradually lost interest in general and took particular pleasure in eating. This caused her to gain considerable weight. It was not until she realized that her husband was ashamed of her appearance that she roused herself and went on a

heroic diet. For practically a year she lived on nothing but milk, fruit and bran and so lost over 100 pounds (45 Kg.). Her continued conflicts, together with the drastic reduction in weight, led to a second, prolonged psychotic episode. This time she was very confused and was often delirious or in a catatonic stupor.

Her recovery was slower than before and was accompanied by the emergence of feelings of hate and aggression. These, it would seem, were a definite gain—an evidence of growth, counterbalancing to some extent her dependence and immaturity. They made possible her subsequent decisive action, for when she found how her husband had handled her affairs during her illness she took matters into her own hands. She acted with initiative and realism: She placed her affairs in the hands of a trust company, obtained legal and spiritual advice and consulted psychiatrists regarding her competency to make a will.

After getting rid of her husband and assuming control of her affairs, she was well and lived happily with her children. She traveled extensively, painted at leisure and became more and more absorbed in her religious devotions. She attended mass and received communion daily. Attempts during these years and subsequently failed to help her face facts objectively, for later events made it evident that she centered in the physician all the needs she had for a human, idealized lover. After her one burst of self-assertion, she fell back into her old habits of day dreaming and shifting responsibility to others. Her wealth and religious beliefs made this easy.

Her absorption in religion and in the physician's person grew apace, for she worried about his salvation and prayed for his conversion to the Catholic faith. As her preoccupation grew more intense, she wrote him many letters, gradually unfolding what she claimed to be God's plan. She said that his real name was "Joseph" and hers "Mary" and that God was making almost daily revelations to her. These included the death of his wife and her husband and her subsequent marriage to the physician. The physician tried to dissuade her in every way possible, pointing out discrepancies and contradictions in her previous predictions and the wishful nature of her disclosures. All these remonstrances, however, only caused her to smile patiently and superiorly. When, by coincidence, the physician's wife died, she became convinced of the truth of her revelations. She became so sure that God was guiding her directly that she even stopped heeding the admonitions of her confessor and finally ceased to seek his counsel. She claimed God had revealed the exact date of her husband's death and made elaborate preparations to gain sufficient grace to save his soul. When he did not die on the date revealed, she consoled herself by believing she had misunderstood God and that he would die just a year later.

Though outwardly she accepted this rationalization, inwardly the shock of the nonfulfilment of her revelation, as well as the physician's disbelief and failure to cooperate, could not be so easily disposed of. She stopped seeing him but continued to write to him. From her letters it is apparent that in her world of dreams and wishes, in the subconscious, she was able to eliminate obstacles and to provide beautiful and romantic solutions of all difficulties. Here her religious fantasies and her wishes joined hands, for to God nothing is impossible. Gradually, she transferred the intensity of her love from the physician to Jesus, for she wrote numerous letters telling of her spiritual experiences, even of her actual experience of mystical marriage with Jesus. Finally, she wrote that through her spiritual union with Christ she would conceive and give birth to a child who would be the physical incarnation of the Third Person of the Trinity, thereby reaching the acme of her aspirations and delusions by equaling the Blessed Mother. She and the physician, still playing the rôles of Mary and Joseph, living in complete continence, were to be married and bring up this child.

When the next year passed without the death of her husband, she must have begun to doubt her whole system of ideas, for shortly after this her daughter reported that the mother was becoming confused. When the physician saw her, she was totally out of touch with reality, stared vaguely into space and apparently did not recognize him. Since she was so agitated, it was necessary to send her

to a sanatorium for safe-keeping and treatment. She remained there several months and was then taken to the western coast, where she is now living. Her husband is managing her affairs here and reports that she is contented. From time to time she has written the physician simple letters of actual occurrences. While she has gradually ceased to address him as "Joseph," she still signs herself as "Mary." It would seem, therefore, that she is improving but has not completely renounced her compensatory religious delusions.

*Comment.*—From the analytic point of view one could say that as a result of conflicts and the responsibilities of life for which she was unprepared she became tired and exhausted, turned her back repeatedly on reality and took refuge in psychotic episodes, regressing to childhood and infantile levels, for those periods were for her the golden age. The family romance did not come up baldly as such, for that would have been too painful. This conflict was avoided by making use of the Holy Family and the ideology of the Church. Her love for her father was gradually transferred, via the physician, to Christ, with whom she achieved ecstatic, mystic union and by whom she was to have a child. Since the father was God, the child was conceived without sin. Her superego was therefore able to join forces with the id, to the great detriment of the ego and its periodic repression during the psychotic episodes. It would seem that in recent years some peace had been achieved between these two divergent tendencies, making possible a fair adjustment to reality while she maintained probably a part of her delusions.

Some light is also thrown in the study of this case on some factors that may play a rôle in spontaneous recoveries from psychotic episodes. The patient emerged from her second attack with definite feelings of hate and aggression, which made her, for the time, much more independent, self-reliant and mature.

#### ART AS A MEANS OF EXPRESSION IN SOME OF THE MAJOR PSYCHOSES AS APPLIED IN OCCUPATIONAL THERAPY. DR. THEOPHIL KLINGMANN, Ann Arbor, Mich.

Creative art seems to depend on inborn qualities. However, it must have an opportunity to present itself and requires a cultural background. Such qualities are often repressed or entirely unconscious. The application of art in occupational therapy in some of the major psychoses, especially in schizophrenia and not infrequently in the depressive (manic-depressive) psychoses, has often given the opportunity to reveal this talent in the form of symbolic pictures, indicating a struggle within the unconscious to attain a higher social level, an important factor, therefore in the mental conflict of the patient. The results of such efforts illustrate the patient's repressed wishes and give the psychiatrist contacts which not infrequently lead to the solution of a problem.

Revelations in creative art by the schizophrenic patient are of value in establishing contacts which otherwise seemed impossible. The various moods of patients are illustrated in pen and ink and pencil sketches of facial expression in portrait, grotesque figures, flowers and landscapes in water colors and oils or hallucinations in clay.

The fifty illustrations presented on the screen have served to reveal delusions of persecution, ideas of influence, hallucinations of sight, sexual cravings, repressive and exalted moods and reactions of repressed wishes.

They have made possible contacts with the mute schizophrenic patient and have given the patient a pleasing and constructive occupation—a means of expression with gratifying results. To the psychiatrist they have furnished valuable contacts, an aid to adjustment and at times a criterion in differential diagnosis.

#### "SEX HORMONES" AND THEIR RELATION TO SCHIZOPHRENIA. DR. R. A. MORTER, Kalamazoo, Mich.

A study of the relationship of the "sex hormones" to schizophrenia was started at the Kalamazoo State Hospital about a year and a half ago. This study was prompted by the prevalence of physical signs of "sex hormone" deficiency in the great majority of schizophrenic men and women. These signs may be described

as follows: Eunuchoid components in physical build or hypoplastic traits, such as dwarfism and stunting of the whole body, may be present. The color of the skin is frequently pale. The primary growth of hair (head and eyebrows) is strong and coarse. The hair on the head is often abundant and shows a tendency to grow down on the forehead, giving the "fur cap" appearance. The growth of secondary hair is usually weak. The sexual drive is weakened. Female schizophrenic subjects frequently present a picture of masculinity, hypertrichosis, hypoplastic traits, amenorrhea and genital hypoplasia.

The chief work has been done with the estrogenic hormones. A norm was established in a group of 63 nurses and college students, who served as controls. In this group the estrogenic substance was found in the premenstrual blood of 94 per cent of the subjects. In similar studies made on 238 schizophrenic women the test for estrogenic substance in the blood gave a negative reaction in 70 per cent of cases. This tremendous disparity between 70 per cent of negative reactions in the group with schizophrenia and 6 per cent in the group used as a control leads one to wonder whether the absence of the estrogenic substance can in any way be an etiologic factor in schizophrenia. Examination of the urine of these patients ruled out the possibility that the estrogenic substance spills through the kidneys and is then absent in the blood. It is believed that the failure to produce the estrogenic substance is due not to disease of the ovary itself but to a pituitary dysfunction, and my associates and I expect to investigate the presence or absence of the gonadotropic principle in these patients in the near future.

Our research suggests that estrogenic therapy might be useful in the treatment of schizophrenia. This has been tried for the past six months but is still in the experimental stage. Therapy was started recently in a group of women with schizophrenia with the hypodermic administration of 2,000 international units of theelin in oil twice a week. The dose was doubled each succeeding week. Weekly tests of the blood and urine for the presence of the estrogenic substance are being made in these cases; at present the dose has reached 64,000 international units, and there is no apparent increase of the estrogenic substance in the urine. The fate of the injected estrogenic substance is still unknown. We are increasing the dose with caution, because of the untoward results anticipated by some investigators, but we hope to be able to increase the dose until the estrogenic substance becomes demonstrable in the blood or until we find a definite increase of the substance in the urine. When this occurs, we shall know that the maximum dose of theelin has been reached. When this dose is reached, we can expect to notice improvement in the symptoms of schizophrenia if a low content or absence of the estrogenic substance in the blood is an etiologic factor in this disease.

In conclusion, I wish to emphasize the following points: (1) the physical signs of "sex hormone" deficiency in schizophrenia; (2) the absence or deficiency of sexual drive in schizophrenic patients; (3) the disparity between the number of negative reactions of the blood to tests for the estrogenic substance in schizophrenic women (70 per cent) and that in subjects used as controls (4 per cent); (4) a definite imbalance of the gonadotropic and gonad-stimulating hormones in schizophrenic women, and (5) the necessity, if the estrogenic substance is to be used experimentally as a therapeutic agent, for large doses to be administered and regulated according to the laboratory data obtained in each case.

## Book Reviews

**The Intellectual Functions of the Frontal Lobes: A Study Based upon Observation of a Man After Partial Bilateral Frontal Lobectomy.**  
By Richard M. Brickner, B.S., M.D. Cloth. Price, \$3.50. Pp. 354, no illustrations. New York: The Macmillan Company, 1936.

This book is an important contribution to the knowledge of that domain in which physiology and psychology meet. No work on apes can fully elucidate the functions of the frontal lobes; it is a strictly human problem. As Tilney says in his preface to Brickner's monograph: "The brains of lower animals can do little more than offer suggestive leads. It is for this reason that every case offering proper and favorable opportunities for investigation must be utilized to the fullest extent." Brickner appreciated his opportunity when Mr. A. (after operation by Dandy, in Baltimore) came to him as a patient. The book tells the story of the patient's life before the tumor of the brain developed and gives a good clinical history of the illness and of the operation for excision of the parasagittal meningioma. Removal of the tumor necessitated amputation of most of both frontal lobes in front of area 6 (i.e., on the two sides the portions removed, as designated in Brodmann's terms, were areas 8, 9, 10, 11, 12, 16, 24, 32, 33, 44, 45, 46 and 47 and probably area 25 but probably none of area 6).

Fourteen months after operation Brickner began his intensive observations of the patient. They were carried out in an unusually thorough manner because of Brickner's appreciation of the importance of the case and were made possible by cooperation on the part of the patient's family. Detailed notes were made by Brickner and his assistant, Dr. Peter Lerner, often with the aid of a stenographer to take long productions verbatim. Thus, there have been gathered the best data available in a case of this kind. The author is to be congratulated on his foresight and assiduity. The main body of the book is made up of these data (pages 35 to 233), published fully, with a few explanatory and interpretative paragraphs, under the following headings:

I. Symptoms in the Intellectual Sphere with Emotional Coloring. (A) Impairment of restraint in controlling or concealing emotion, as indicated by: boasting, self-aggrandizement and free expression of mild hostility and of angry, aggressive, negativistic and puerile impulses. Other authors have described these phenomena in terms such as impairment of "social sense," "character and personality change," impairment of "moral sense" and *Witzelsucht*. (B) Preservation of restraint.

II. Symptoms in the Intellectual Sphere Without Emotional Coloring. Limitation of the capacity to associate or synthesize mental engrams to a complex degree (primary phenomenon). This is indicated by difficulty in maintaining fixation of attention (distractibility), impairment of the capacity to select and segregate units of intellectual activity (particularization), impairment of retention (a secondary phenomenon) and impairment of learning capacity.

Additional phenomena were disturbances in judgment, critique, abstractive ability, appreciation of situations, capacity to evade, capacity to bluff, sense of humor, orientation and initiative. The presence of stereotypy of thinking and slowing of cerebration were positive symptoms. There were also observed such symptoms as: lack of insight into the gravity of the situation, euphoria, use of jargon, compulsiveness and incontinence. Aphasia was seldom noted, the only common symptom suggestive of aphasia being perseveration.

Many formal psychologic tests were given. These are recorded in pages 233 to 266. This factual part of the book is a record unique in medical literature and can be studied and evaluated by students of anatomy, physiology and psychology.

The exposition in part III, entitled "Interpretation" (pages 269 to 318), is open to argument and to difference of opinion. The author's point of view, however, is simply and moderately expressed and commands respect, even if it does not always

cause conviction. Two passages (pages 269 to 270) present his interpretation: "There is nothing to indicate any change in the fundamental character of any of the processes of A's mind; nothing really new has developed in A's personality and nothing old has disappeared, but there are more of some old characteristics, and less of others. According to his family and to the friends who have read parts of the record, A is essentially the same type of person now as he was prior to his illness. A's record also shows that there is no actual loss of any interpretable function; there is decrease or increase of activation in each instance. The activity of every function could easily be more greatly diminished or more greatly exaggerated; indeed, each symptom is actually more pronounced at one time than another. The exercise of restraint, for example, is not entirely in abeyance; it appears in varying degree on different occasions. *Therefore, we are dealing fundamentally with a quantitative, rather than a qualitative, change.*

"Of all the fundamental functions there is one which appears to be of special importance in the interpretation of A's productions—the ability to synthesize simple thought processes into more complex structures. It seems possible to explain many of the phenomena on the basis of a diminution in this synthesizing capacity.

"This reduction in synthesizing capacity may reveal itself symptomatically in either of two ways: (1) By manifestations referable to the separate activation of simple engrammatic units which formerly were synthesized. (2) By defects in complex, synthetic functions (such as restraint) whose existence depends upon the synthesis of simple engrammatic units."

Some controversial points are well discussed, and the review of the literature is thorough and well documented. In discussing whether or not emotional reactions may be "represented" in the frontal lobes, Brickner says (pages 278 to 279): "Although the motivations which prompt the individual are emotional in nature, the processes of examining them (limited as they may be), of appreciating the consequences of their expression, of choosing which of a series of consequences is preferable, and of planning the attempt to attain that choice, appear to be as much of an intellectual nature as any other processes of planning and ordination. They require memory, and elaboration (or synthesis) of simple elements into more complicated forms of idea. Hence restraint is, in itself, the product of intellectual operations."

The reviewer is tempted to pick out the word "elaboration" as the key to this paragraph and to add that the very process of association and elaboration takes time, brings in data of past experience and perhaps is the intellectual process. Indeed, it could not take place without "restraint." It seems to be the very thing that makes the behavior of an adult man superior to that of a child or a monkey. Therefore it is difficult to agree entirely with Brickner when (on page 303) he says: "From the point of view of the intellect, then, the frontal cortex may be thought of as tissue that enriches the intellect immensely, by virtue of multiplication of the associative possibilities. The frontal lobes would then be, from a biological standpoint, luxuries; intellectual activity of a fairly high order can proceed without them."

Certainly the most important thing one possesses cannot be considered a "luxury"! There are plenty of persons in the world who have little enough richness of intellect—"morons" or "dull normals," if one will—but there is a need for leadership, and the superior adult is a necessity, not a luxury.

On page 315 is the statement: "Perhaps the most mystifying of the special symptoms is the patient's lack of appreciation of the gravity of the situation." After carefully reading the book, this does not seem mystifying. Why is not a generally euphoric mood, a lack of appreciation of "gravity," just what one would expect from loss of the power of complex synthesis? One is grave when one weighs evidence, looks ahead and is judicious. These were things this patient could not do well.

Of particular interest to analytic psychologists will be the observation (pages 316 to 317) "that A's sexual activities—which were normal insofar as can be learned, excepting directly after his marriage—have regressed to a masturbatory

level. Merely phrasing this phenomenon as a psychological regression does not explain it. It is inescapable that, in A, the advance to an adult sexual level was accomplished, at least in part, by virtue of functions in which the frontal lobes were concerned . . . But it is notable that the reproductive urge, fundamentally important as it is, should be so severely disturbed by destruction of the newest portion of the nervous system."

The reviewer applauds Brickner's avoidance of "the many-sided term 'inhibition'." Too long has psychology been embarrassed and muddled by the use of undefined and undefinable terms. In this book the author says what he means in detail, even if it takes several pages, and the use of terms and of English is excellent throughout.

"Summarizing, it may be said that all of the interpretable changes may be explained by a diminution in the function of the synthesis of simple mental engrammes into more complex ones. Thus there are produced disturbances depending upon the separate activation of relatively simple units which formerly were synthesized, and also disturbances in complex derivative faculties whose existence depends upon such synthesis. Hence, the changes are fundamentally quantitative, and not qualitative in character [page 289]."

**Objective and Experimental Psychiatry.** By D. Ewen Cameron. Cloth, \$3. Pp. 271, no illustrations. New York: The Macmillan Company, 1935.

Cameron stresses the importance of basing psychiatric studies on experimentation and quantitation. Uncontrolled observations with conventionalization and projection influencing the interpretation and with overemphasis on conscious activities often lead away from objective studies of basic causes. Psychiatry should be "dehumanized" and concepts of the patient built up from verifiable facts about his functions.

Cameron reviews various experimental and quantitative procedures which are being carried out. He summarizes the present status and contributions of intelligence testing and personality studies, of experimentation on animals—particularly that of Pavlov—and of studies in heredity. He presents briefly, but inclusively, physiologic tests in relation to mental disease. He discusses the simpler principles of statistics and emphasizes their importance.

The book is valuable as a concise, readable review, with a comprehensive bibliography. It leaves one, however, with the feeling that a human being can never be synthesized from studies of the functions of his parts. Such studies must still be supplemented by, and interpreted in, the light of personal observations of the organism functioning in its total situation.

**Guiding Your Life: With Psychology as a Key.** By Josephine A. Jackson, M.D. Price, \$2.50. Pp. 352, no illustrations. New York: D. Appleton-Century Company, Inc., 1937.

In style and point of view this book suggests the "personal advice" column. Its tone is sentimental and its subject-matter inaccurate. Particularly, it goes far beyond established facts in emphasizing the functions of the endocrine system. A degree of "poetic license" might be justified in such volumes as this if their purpose were practicable and valuable. However, it seems unlikely that the reader with his individual problems can be effectively guided by such compilations of arbitrary precepts. And if such guidance were possible, it is questionable whether the resulting smug optimism would be either individually healthy or socially tolerable.